

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
20 June 2002 (20.06.2002)

PCT

(10) International Publication Number
WO 02/47534 A2

- (51) International Patent Classification⁷: **A61B**
- (21) International Application Number: PCT/US01/47576
- (22) International Filing Date:
30 November 2001 (30.11.2001)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
09/735,705 12 December 2000 (12.12.2000) US
09/850,716 7 May 2001 (07.05.2001) US
09/897,778 28 June 2001 (28.06.2001) US

(71) Applicant (for all designated States except US): **CORIXA CORPORATION** [US/US]; 1124 Columbia Street, Suite 200, Seattle, WA 98104 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **WANG, Tongtong** [US/US]; 8049 N.E. 28th Street, Medina, WA 98039 (US). **WANG, Aijun** [CN/US]; 3106 213th Place S.E., Issaquah, WA 98029 (US). **SKEIKY, Yasir, A.W.** [LB/US]; 15106 S.E. 47th Place, Bellevue, WA 98006 (US). **LI, Samuel, X.** [US/US]; 3608 175th Court N.E., Redmond, WA 98052 (US). **KALOS, Michael, D.** [US/US]; 8116 Dayton Avenue N., Seattle, WA 98103 (US). **HENDERSON, Robert, A.** [US/US]; 8904 192nd Street S.W., Edmonds, WA 98026 (US). **MCNEILL, Patricia, D.** [US/US]; 1333 South 290th Place, Federal Way, WA 98003 (US). **FANGER, Neil** [US/US]; 3648 Whitman Avenue N., A100, Seattle, WA 98103 (US). **RETTTER, Marc, W.** [US/US]; 33402 N.E. 43rd Place, Carnation, WA 98014 (US). **DURHAM, Margarita** [US/US]; 3444 36th Avenue W., Seattle, WA 98199 (US). **FANGER, Gary, R.** [US/US]; 15906 29th Drive S.E., Mill Creek, WA 98012

(US). **VEDVICK, Thomas, S.** [US/US]; 124 S. 300th Place, Federal Way, WA 98003 (US). **CARTER, Darriek** [US/US]; 321 Summit Ave. E., Seattle, WA 98102 (US). **WATANABE, Yoshihiro** [JP/US]; 2266 78th Avenue S.E., Mercer Island, WA 98040 (US). **PECKHAM, David, W.** [US/US]; 903 9th Avenue, Apt. #31, Seattle, WA 98104 (US). **CAI, Feng** [US/US]; 5403 N.E. 197th, Lake Forest Park, WA 98155 (US). **FOY, Teresa, M.** [US/US]; 2104 S. 277th Place, Federal Way, WA 98003 (US).

(74) Agents: **CHRISTIANSEN, William, T.**; Seed Intellectual Property Law Group PLLC, Suite 6300, 701 Fifth Avenue, Seattle, WA 98104-7092 et al. (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— without international search report and to be republished upon receipt of that report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER

(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, particularly lung cancer, are disclosed. Illustrative compositions comprise one or more lung tumor polypeptides, immunogenic portions thereof, polynucleotides that encode such polypeptides, antigen presenting cell that expresses such polypeptides, and T cells that are specific for cells expressing such polypeptides. The disclosed compositions are useful, for example, in the diagnosis, prevention and/or treatment of diseases, particularly lung cancer.



WO 02/47534 A2

COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF LUNG CANCER

TECHNICAL FIELD OF THE INVENTION

The present invention relates generally to therapy and diagnosis of
5 cancer, such as lung cancer. The invention is more specifically related to polypeptides,
comprising at least a portion of a lung tumor protein, and to polynucleotides encoding
such polypeptides. Such polypeptides and polynucleotides are useful in pharmaceutical
compositions, *e.g.*, vaccines, and other compositions for the diagnosis and treatment of
lung cancer.

10 BACKGROUND OF THE INVENTION

Field of the Invention

Cancer is a significant health problem throughout the world. Although
advances have been made in detection and therapy of cancer, no vaccine or other
universally successful method for prevention and/or treatment is currently available.
15 Current therapies, which are generally based on a combination of chemotherapy or
surgery and radiation, continue to prove inadequate in many patients.

Description of Related Art

Lung cancer is the primary cause of cancer death among both men and
women in the U.S., with an estimated 172,000 new cases being reported in 1994. The
20 five-year survival rate among all lung cancer patients, regardless of the stage of disease
at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among
cases detected while the disease is still localized. However, only 16% of lung cancers
are discovered before the disease has spread.

In spite of considerable research into therapies for these and other
25 cancers, lung cancer remains difficult to diagnose and treat effectively. Accordingly,
there is a need in the art for improved methods for detecting and treating such cancers.
The present invention fulfills these needs and further provides other related advantages.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides polynucleotide compositions comprising a sequence selected from the group consisting of:

- (a) sequences provided in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;
- (b) complements of the sequences provided in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;
- (c) sequences consisting of at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 75 and 100 contiguous residues of a sequence provided in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;
- (d) sequences that hybridize to a sequence provided in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467, under moderate or highly stringent conditions;
- (e) sequences having at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identity to a sequence of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30,

32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 5 434, 442, 447, 450 and 467; and

(f) degenerate variants of a sequence provided in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 10 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467.

In one preferred embodiment, the polynucleotide compositions of the invention are expressed in at least about 20%, more preferably in at least about 30%, and most preferably in at least about 50% of lung tumors samples tested, at a level that 15 is at least about 2-fold, preferably at least about 5-fold, and most preferably at least about 10-fold higher than that for normal tissues.

The present invention, in another aspect, provides polypeptide compositions comprising an amino acid sequence that is encoded by a polynucleotide sequence described above.

20 The present invention further provides polypeptide compositions comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO:152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344, 346, 350, 357, 361, 363, 365, 367, 369, 376-382, 387-419, 423, 427, 430, 433, 441, 443, 446, 449, 451-466 and 468-469.

25 In certain preferred embodiments, the polypeptides and/or polynucleotides of the present invention are immunogenic, *i.e.*, they are capable of eliciting an immune response, particularly a humoral and/or cellular immune response, as further described herein.

The present invention further provides fragments, variants and/or 30 derivatives of the disclosed polypeptide and/or polynucleotide sequences, wherein the fragments, variants and/or derivatives preferably have a level of immunogenic activity

of at least about 50%, preferably at least about 70% and more preferably at least about 90% of the level of immunogenic activity of a polypeptide sequence set forth in SEQ ID NO:152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344, 346, 350, 357, 361, 363, 365, 367, 369, 376-382, 387-419, 423, 427, 430, 433, 441, 443, 446, 449 and
5 451-466, or a polypeptide sequence encoded by a polynucleotide sequence set forth in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364,
10 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467.

The present invention further provides polynucleotides that encode a polypeptide described above, expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

Within other aspects, the present invention provides pharmaceutical
15 compositions comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

Within a related aspect of the present invention, the pharmaceutical compositions, *e.g.*, vaccine compositions, are provided for prophylactic or therapeutic applications. Such compositions generally comprise an immunogenic polypeptide or
20 polynucleotide of the invention and an immunostimulant, such as an adjuvant.

The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a polypeptide of the present invention, or a fragment thereof; and (b) a physiologically acceptable carrier.

25 Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Illustrative antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, pharmaceutical compositions are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins
5 that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins, typically in the form of pharmaceutical compositions, *e.g.*, vaccine compositions, comprising a physiologically acceptable carrier and/or an immunostimulant. The fusions proteins may comprise multiple immunogenic polypeptides or portions/variants thereof, as described herein, and may further comprise
10 one or more polypeptide segments for facilitating the expression, purification and/or immunogenicity of the polypeptide(s).

Within further aspects, the present invention provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient, comprising administering a pharmaceutical composition described herein. The
15 patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
20 patient a pharmaceutical composition as recited above. The patient may be afflicted with lung cancer, in which case the methods provide treatment for the disease, or patient considered at risk for such a disease may be treated prophylactically.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological
25 sample with T cells that specifically react with a polypeptide of the present invention, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological
30 sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a polypeptide of the present invention, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that
5 expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a
10 patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating CD4⁺ and/or CD8⁺ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of polypeptide disclosed herein; (ii) a
15 polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer, preferably a lung cancer, in a patient comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of
20 polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps
30 of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the

sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the
5 patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b)
10 detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one
15 oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a polypeptide of the present invention; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b)
20 using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as
30 monoclonal antibodies, that bind to a polypeptide as described above, as well as

diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

SEQUENCE IDENTIFIERS

- SEQ ID NO:1 is the determined cDNA sequence for LST-S1-2
SEQ ID NO:2 is the determined cDNA sequence for LST-S1-28
10 SEQ ID NO:3 is the determined cDNA sequence for LST-S1-90
SEQ ID NO:4 is the determined cDNA sequence for LST-S1-144
SEQ ID NO:5 is the determined cDNA sequence for LST-S1-133
SEQ ID NO:6 is the determined cDNA sequence for LST-S1-169
SEQ ID NO:7 is the determined cDNA sequence for LST-S2-6
15 SEQ ID NO:8 is the determined cDNA sequence for LST-S2-11
SEQ ID NO:9 is the determined cDNA sequence for LST-S2-17
SEQ ID NO:10 is the determined cDNA sequence for LST-S2-25
SEQ ID NO:11 is the determined cDNA sequence for LST-S2-39
SEQ ID NO:12 is a first determined cDNA sequence for LST-S2-43
20 SEQ ID NO:13 is a second determined cDNA sequence for LST-S2-43
SEQ ID NO:14 is the determined cDNA sequence for LST-S2-65
SEQ ID NO:15 is the determined cDNA sequence for LST-S2-68
SEQ ID NO:16 is the determined cDNA sequence for LST-S2-72
SEQ ID NO:17 is the determined cDNA sequence for LST-S2-74
25 SEQ ID NO:18 is the determined cDNA sequence for LST-S2-103
SEQ ID NO:19 is the determined cDNA sequence for LST-S2-N1-1F
SEQ ID NO:20 is the determined cDNA sequence for LST-S2-N1-2A
SEQ ID NO:21 is the determined cDNA sequence for LST-S2-N1-4H
SEQ ID NO:22 is the determined cDNA sequence for LST-S2-N1-5A
30 SEQ ID NO:23 is the determined cDNA sequence for LST-S2-N1-6B

- SEQ ID NO:24 is the determined cDNA sequence for LST-S2-N1-7B
SEQ ID NO:25 is the determined cDNA sequence for LST-S2-N1-7H
SEQ ID NO:26 is the determined cDNA sequence for LST-S2-N1-8A
SEQ ID NO:27 is the determined cDNA sequence for LST-S2-N1-8D
5 SEQ ID NO:28 is the determined cDNA sequence for LST-S2-N1-9A
SEQ ID NO:29 is the determined cDNA sequence for LST-S2-N1-9E
SEQ ID NO:30 is the determined cDNA sequence for LST-S2-N1-10A
SEQ ID NO:31 is the determined cDNA sequence for LST-S2-N1-10G
SEQ ID NO:32 is the determined cDNA sequence for LST-S2-N1-11A
10 SEQ ID NO:33 is the determined cDNA sequence for LST-S2-N1-12C
SEQ ID NO:34 is the determined cDNA sequence for LST-S2-N1-12E
SEQ ID NO:35 is the determined cDNA sequence for LST-S2-B1-3D
SEQ ID NO:36 is the determined cDNA sequence for LST-S2-B1-6C
SEQ ID NO:37 is the determined cDNA sequence for LST-S2-B1-5D
15 SEQ ID NO:38 is the determined cDNA sequence for LST-S2-B1-5F
SEQ ID NO:39 is the determined cDNA sequence for LST-S2-B1-6G
SEQ ID NO:40 is the determined cDNA sequence for LST-S2-B1-8A
SEQ ID NO:41 is the determined cDNA sequence for LST-S2-B1-8D
SEQ ID NO:42 is the determined cDNA sequence for LST-S2-B1-10A
20 SEQ ID NO:43 is the determined cDNA sequence for LST-S2-B1-9B
SEQ ID NO:44 is the determined cDNA sequence for LST-S2-B1-9F
SEQ ID NO:45 is the determined cDNA sequence for LST-S2-B1-12D
SEQ ID NO:46 is the determined cDNA sequence for LST-S2-I2-2B
SEQ ID NO:47 is the determined cDNA sequence for LST-S2-I2-5F
25 SEQ ID NO:48 is the determined cDNA sequence for LST-S2-I2-6B
SEQ ID NO:49 is the determined cDNA sequence for LST-S2-I2-7F
SEQ ID NO:50 is the determined cDNA sequence for LST-S2-I2-8G
SEQ ID NO:51 is the determined cDNA sequence for LST-S2-I2-9E
SEQ ID NO:52 is the determined cDNA sequence for LST-S2-I2-12B
30 SEQ ID NO:53 is the determined cDNA sequence for LST-S2-H2-2C
SEQ ID NO:54 is the determined cDNA sequence for LST-S2-H2-1G

- SEQ ID NO:55 is the determined cDNA sequence for LST-S2-H2-4G
SEQ ID NO:56 is the determined cDNA sequence for LST-S2-H2-3H
SEQ ID NO:57 is the determined cDNA sequence for LST-S2-H2-5G
SEQ ID NO:58 is the determined cDNA sequence for LST-S2-H2-9B
5 SEQ ID NO:59 is the determined cDNA sequence for LST-S2-H2-10H
SEQ ID NO:60 is the determined cDNA sequence for LST-S2-H2-12D
SEQ ID NO: 61 is the determined cDNA sequence for LST-S3-2
SEQ ID NO: 62 is the determined cDNA sequence for LST-S3-4
SEQ ID NO: 63 is the determined cDNA sequence for LST-S3-7
10 SEQ ID NO: 64 is the determined cDNA sequence for LST-S3-8
SEQ ID NO: 65 is the determined cDNA sequence for LST-S3-12
SEQ ID NO: 66 is the determined cDNA sequence for LST-S3-13
SEQ ID NO: 67 is the determined cDNA sequence for LST-S3-14
SEQ ID NO: 68 is the determined cDNA sequence for LST-S3-16
15 SEQ ID NO: 69 is the determined cDNA sequence for LST-S3-21
SEQ ID NO: 70 is the determined cDNA sequence for LST-S3-22
SEQ ID NO: 71 is the determined cDNA sequence for LST-S1-7
SEQ ID NO: 72 is the determined cDNA sequence for LST-S1-A-1E
SEQ ID NO: 73 is the determined cDNA sequence for LST-S1-A-1G
20 SEQ ID NO: 74 is the determined cDNA sequence for LST-S1-A-3E
SEQ ID NO: 75 is the determined cDNA sequence for LST-S1-A-4E
SEQ ID NO: 76 is the determined cDNA sequence for LST-S1-A-6D
SEQ ID NO: 77 is the determined cDNA sequence for LST-S1-A-8D
SEQ ID NO: 78 is the determined cDNA sequence for LST-S1-A-10A
25 SEQ ID NO: 79 is the determined cDNA sequence for LST-S1-A-10C
SEQ ID NO: 80 is the determined cDNA sequence for LST-S1-A-9D
SEQ ID NO: 81 is the determined cDNA sequence for LST-S1-A-10D
SEQ ID NO: 82 is the determined cDNA sequence for LST-S1-A-9H
SEQ ID NO: 83 is the determined cDNA sequence for LST-S1-A-11D
30 SEQ ID NO: 84 is the determined cDNA sequence for LST-S1-A-12D
SEQ ID NO: 85 is the determined cDNA sequence for LST-S1-A-11E

- SEQ ID NO: 86 is the determined cDNA sequence for LST-S1-A-12E
- SEQ ID NO: 87 is the determined cDNA sequence for L513S (T3).
- SEQ ID NO: 88 is the determined cDNA sequence for L513S contig 1.
- SEQ ID NO: 89 is a first determined cDNA sequence for L514S.
- 5 SEQ ID NO: 90 is a second determined cDNA sequence for L514S.
- SEQ ID NO: 91 is a first determined cDNA sequence for L516S.
- SEQ ID NO: 92 is a second determined cDNA sequence for L516S.
- SEQ ID NO: 93 is the determined cDNA sequence for L517S.
- SEQ ID NO: 94 is the extended cDNA sequence for LST-S1-169 (also known as
- 10 L519S).
- SEQ ID NO: 95 is a first determined cDNA sequence for L520S.
- SEQ ID NO: 96 is a second determined cDNA sequence for L520S.
- SEQ ID NO: 97 is a first determined cDNA sequence for L521S.
- SEQ ID NO: 98 is a second determined cDNA sequence for L521S.
- 15 SEQ ID NO: 99 is the determined cDNA sequence for L522S.
- SEQ ID NO: 100 is the determined cDNA sequence for L523S.
- SEQ ID NO: 101 is the determined cDNA sequence for L524S.
- SEQ ID NO: 102 is the determined cDNA sequence for L525S.
- SEQ ID NO: 103 is the determined cDNA sequence for L526S.
- 20 SEQ ID NO: 104 is the determined cDNA sequence for L527S.
- SEQ ID NO: 105 is the determined cDNA sequence for L528S.
- SEQ ID NO: 106 is the determined cDNA sequence for L529S.
- SEQ ID NO: 107 is a first determined cDNA sequence for L530S.
- SEQ ID NO: 108 is a second determined cDNA sequence for L530S.
- 25 SEQ ID NO: 109 is the determined full-length cDNA sequence for L531S short form
- SEQ ID NO: 110 is the amino acid sequence encoded by SEQ ID NO: 109.
- SEQ ID NO: 111 is the determined full-length cDNA sequence for L531S long form
- SEQ ID NO: 112 is the amino acid sequence encoded by SEQ ID NO: 111.
- SEQ ID NO: 113 is the determined full-length cDNA sequence for L520S.
- 30 SEQ ID NO: 114 is the amino acid sequence encoded by SEQ ID NO: 113.
- SEQ ID NO: 115 is the determined cDNA sequence for contig 1.

- SEQ ID NO: 116 is the determined cDNA sequence for contig 3.
SEQ ID NO: 117 is the determined cDNA sequence for contig 4.
SEQ ID NO: 118 is the determined cDNA sequence for contig 5.
SEQ ID NO: 119 is the determined cDNA sequence for contig 7.
- 5 SEQ ID NO: 120 is the determined cDNA sequence for contig 8.
SEQ ID NO: 121 is the determined cDNA sequence for contig 9.
SEQ ID NO: 122 is the determined cDNA sequence for contig 10.
SEQ ID NO: 123 is the determined cDNA sequence for contig 12.
SEQ ID NO: 124 is the determined cDNA sequence for contig 11.
- 10 SEQ ID NO: 125 is the determined cDNA sequence for contig 13 (also known as L761P).
SEQ ID NO: 126 is the determined cDNA sequence for contig 15.
SEQ ID NO: 127 is the determined cDNA sequence for contig 16.
SEQ ID NO: 128 is the determined cDNA sequence for contig 17.
- 15 SEQ ID NO: 129 is the determined cDNA sequence for contig 19.
SEQ ID NO: 130 is the determined cDNA sequence for contig 20.
SEQ ID NO: 131 is the determined cDNA sequence for contig 22.
SEQ ID NO: 132 is the determined cDNA sequence for contig 24.
SEQ ID NO: 133 is the determined cDNA sequence for contig 29.
- 20 SEQ ID NO: 134 is the determined cDNA sequence for contig 31.
SEQ ID NO: 135 is the determined cDNA sequence for contig 33.
SEQ ID NO: 136 is the determined cDNA sequence for contig 38.
SEQ ID NO: 137 is the determined cDNA sequence for contig 39.
SEQ ID NO: 138 is the determined cDNA sequence for contig 41.
- 25 SEQ ID NO: 139 is the determined cDNA sequence for contig 43.
SEQ ID NO: 140 is the determined cDNA sequence for contig 44.
SEQ ID NO: 141 is the determined cDNA sequence for contig 45.
SEQ ID NO: 142 is the determined cDNA sequence for contig 47.
SEQ ID NO: 143 is the determined cDNA sequence for contig 48.
- 30 SEQ ID NO: 144 is the determined cDNA sequence for contig 49.
SEQ ID NO: 145 is the determined cDNA sequence for contig 50.

- SEQ ID NO: 146 is the determined cDNA sequence for contig 53.
SEQ ID NO: 147 is the determined cDNA sequence for contig 54.
SEQ ID NO: 148 is the determined cDNA sequence for contig 56.
SEQ ID NO: 149 is the determined cDNA sequence for contig 57.
- 5 SEQ ID NO: 150 is the determined cDNA sequence for contig 58.
SEQ ID NO: 151 is the full-length cDNA sequence for L530S.
SEQ ID NO: 152 is the amino acid sequence encoded by SEQ ID NO: 151
SEQ ID NO: 153 is the full-length cDNA sequence of a first variant of L514S
SEQ ID NO: 154 is the full-length cDNA sequence of a second variant of L514S
- 10 SEQ ID NO: 155 is the amino acid sequence encoded by SEQ ID NO: 153.
SEQ ID NO: 156 is the amino acid sequence encoded by SEQ ID NO: 154.
SEQ ID NO: 157 is the determined cDNA sequence for contig 59.
SEQ ID NO: 158 is the full-length cDNA sequence for L763P (also referred to as contig 22).
- 15 SEQ ID NO: 159 is the amino acid sequence encoded by SEQ ID NO: 158.
SEQ ID NO: 160 is the full-length cDNA sequence for L762P (also referred to as contig 17).
SEQ ID NO: 161 is the amino acid sequence encoded by SEQ ID NO: 160.
SEQ ID NO: 162 is the determined cDNA sequence for L515S.
- 20 SEQ ID NO: 163 is the full-length cDNA sequence of a first variant of L524S.
SEQ ID NO: 164 is the full-length cDNA sequence of a second variant of L524S.
SEQ ID NO: 165 is the amino acid sequence encoded by SEQ ID NO: 163.
SEQ ID NO: 166 is the amino acid sequence encoded by SEQ ID NO: 164.
SEQ ID NO: 167 is the full-length cDNA sequence of a first variant of L762P.
- 25 SEQ ID NO: 168 is the full-length cDNA sequence of a second variant of L762P.
SEQ ID NO: 169 is the amino acid sequence encoded by SEQ ID NO: 167.
SEQ ID NO: 170 is the amino acid sequence encoded by SEQ ID NO: 168.
SEQ ID NO: 171 is the full-length cDNA sequence for L773P (also referred to as contig 56).
- 30 SEQ ID NO: 172 is the amino acid sequence encoded by SEQ ID NO: 171.
SEQ ID NO: 173 is an extended cDNA sequence for L519S.

- SEQ ID NO: 174 is the amino acid sequence encoded by SEQ ID NO: 174.
SEQ ID NO: 175 is the full-length cDNA sequence for L523S.
SEQ ID NO: 176 is the amino acid sequence encoded by SEQ ID NO: 175.
SEQ ID NO: 177 is the determined cDNA sequence for LST-sub5-7A.
- 5 SEQ ID NO: 178 is the determined cDNA sequence for LST-sub5-8G.
SEQ ID NO: 179 is the determined cDNA sequence for LST-sub5-8H.
SEQ ID NO: 180 is the determined cDNA sequence for LST-sub5-10B.
SEQ ID NO: 181 is the determined cDNA sequence for LST-sub5-10H.
SEQ ID NO: 182 is the determined cDNA sequence for LST-sub5-12B.
- 10 SEQ ID NO: 183 is the determined cDNA sequence for LST-sub5-11C.
SEQ ID NO: 184 is the determined cDNA sequence for LST-sub6-1c.
SEQ ID NO: 185 is the determined cDNA sequence for LST-sub6-2f.
SEQ ID NO: 186 is the determined cDNA sequence for LST-sub6-2G.
SEQ ID NO: 187 is the determined cDNA sequence for LST-sub6-4d.
- 15 SEQ ID NO: 188 is the determined cDNA sequence for LST-sub6-4e.
SEQ ID NO: 189 is the determined cDNA sequence for LST-sub6-4f.
SEQ ID NO: 190 is the determined cDNA sequence for LST-sub6-3h.
SEQ ID NO: 191 is the determined cDNA sequence for LST-sub6-5d.
SEQ ID NO: 192 is the determined cDNA sequence for LST-sub6-5h.
- 20 SEQ ID NO: 193 is the determined cDNA sequence for LST-sub6-6h.
SEQ ID NO: 194 is the determined cDNA sequence for LST-sub6-7a.
SEQ ID NO: 195 is the determined cDNA sequence for LST-sub6-8a.
SEQ ID NO: 196 is the determined cDNA sequence for LST-sub6-7d.
SEQ ID NO: 197 is the determined cDNA sequence for LST-sub6-7e.
- 25 SEQ ID NO: 198 is the determined cDNA sequence for LST-sub6-8e.
SEQ ID NO: 199 is the determined cDNA sequence for LST-sub6-7g.
SEQ ID NO: 200 is the determined cDNA sequence for LST-sub6-9f.
SEQ ID NO: 201 is the determined cDNA sequence for LST-sub6-9h.
SEQ ID NO: 202 is the determined cDNA sequence for LST-sub6-11b.
- 30 SEQ ID NO: 203 is the determined cDNA sequence for LST-sub6-11c.
SEQ ID NO: 204 is the determined cDNA sequence for LST-sub6-12c.

- SEQ ID NO: 205 is the determined cDNA sequence for LST-sub6-12e.
SEQ ID NO: 206 is the determined cDNA sequence for LST-sub6-12f.
SEQ ID NO: 207 is the determined cDNA sequence for LST-sub6-11g.
SEQ ID NO: 208 is the determined cDNA sequence for LST-sub6-12g.
5 SEQ ID NO: 209 is the determined cDNA sequence for LST-sub6-12h.
SEQ ID NO: 210 is the determined cDNA sequence for LST-sub6-II-1a.
SEQ ID NO: 211 is the determined cDNA sequence for LST-sub6-II-2b.
SEQ ID NO: 212 is the determined cDNA sequence for LST-sub6-II-2g.
SEQ ID NO: 213 is the determined cDNA sequence for LST-sub6-II-1h.
10 SEQ ID NO: 214 is the determined cDNA sequence for LST-sub6-II-4a.
SEQ ID NO: 215 is the determined cDNA sequence for LST-sub6-II-4b.
SEQ ID NO: 216 is the determined cDNA sequence for LST-sub6-II-3e.
SEQ ID NO: 217 is the determined cDNA sequence for LST-sub6-II-4f.
SEQ ID NO: 218 is the determined cDNA sequence for LST-sub6-II-4g.
15 SEQ ID NO: 219 is the determined cDNA sequence for LST-sub6-II-4h.
SEQ ID NO: 220 is the determined cDNA sequence for LST-sub6-II-5c.
SEQ ID NO: 221 is the determined cDNA sequence for LST-sub6-II-5e.
SEQ ID NO: 222 is the determined cDNA sequence for LST-sub6-II-6f.
SEQ ID NO: 223 is the determined cDNA sequence for LST-sub6-II-5g.
20 SEQ ID NO: 224 is the determined cDNA sequence for LST-sub6-II-6g.
SEQ ID NO: 225 is the amino acid sequence for L528S.
SEQ ID NO: 226-251 are synthetic peptides derived from L762P.
SEQ ID NO: 252 is the expressed amino acid sequence of L514S.
SEQ ID NO: 253 is the DNA sequence corresponding to SEQ ID NO: 252.
25 SEQ ID NO: 254 is the DNA sequence of a L762P expression construct.
SEQ ID NO: 255 is the determined cDNA sequence for clone 23785.
SEQ ID NO: 256 is the determined cDNA sequence for clone 23786.
SEQ ID NO: 257 is the determined cDNA sequence for clone 23788.
SEQ ID NO: 258 is the determined cDNA sequence for clone 23790.
30 SEQ ID NO: 259 is the determined cDNA sequence for clone 23793.
SEQ ID NO: 260 is the determined cDNA sequence for clone 23794.

- SEQ ID NO: 261 is the determined cDNA sequence for clone 23795.
SEQ ID NO: 262 is the determined cDNA sequence for clone 23796.
SEQ ID NO: 263 is the determined cDNA sequence for clone 23797.
SEQ ID NO: 264 is the determined cDNA sequence for clone 23798.
5 SEQ ID NO: 265 is the determined cDNA sequence for clone 23799.
SEQ ID NO: 266 is the determined cDNA sequence for clone 23800.
SEQ ID NO: 267 is the determined cDNA sequence for clone 23802.
SEQ ID NO: 268 is the determined cDNA sequence for clone 23803.
SEQ ID NO: 269 is the determined cDNA sequence for clone 23804.
10 SEQ ID NO: 270 is the determined cDNA sequence for clone 23805.
SEQ ID NO: 271 is the determined cDNA sequence for clone 23806.
SEQ ID NO: 272 is the determined cDNA sequence for clone 23807.
SEQ ID NO: 273 is the determined cDNA sequence for clone 23808.
SEQ ID NO: 274 is the determined cDNA sequence for clone 23809.
15 SEQ ID NO: 275 is the determined cDNA sequence for clone 23810.
SEQ ID NO: 276 is the determined cDNA sequence for clone 23811.
SEQ ID NO: 277 is the determined cDNA sequence for clone 23812.
SEQ ID NO: 278 is the determined cDNA sequence for clone 23813.
SEQ ID NO: 279 is the determined cDNA sequence for clone 23815.
20 SEQ ID NO: 280 is the determined cDNA sequence for clone 25298.
SEQ ID NO: 281 is the determined cDNA sequence for clone 25299.
SEQ ID NO: 282 is the determined cDNA sequence for clone 25300.
SEQ ID NO: 283 is the determined cDNA sequence for clone 25301.
SEQ ID NO: 284 is the determined cDNA sequence for clone 25304.
25 SEQ ID NO: 285 is the determined cDNA sequence for clone 25309.
SEQ ID NO: 286 is the determined cDNA sequence for clone 25312.
SEQ ID NO: 287 is the determined cDNA sequence for clone 25317.
SEQ ID NO: 288 is the determined cDNA sequence for clone 25321.
SEQ ID NO: 289 is the determined cDNA sequence for clone 25323.
30 SEQ ID NO: 290 is the determined cDNA sequence for clone 25327.
SEQ ID NO: 291 is the determined cDNA sequence for clone 25328.

- SEQ ID NO:292 is the determined cDNA sequence for clone 25332.
SEQ ID NO:293 is the determined cDNA sequence for clone 25333.
SEQ ID NO:294 is the determined cDNA sequence for clone 25336.
SEQ ID NO:295 is the determined cDNA sequence for clone 25340.
- 5 SEQ ID NO:296 is the determined cDNA sequence for clone 25342.
SEQ ID NO:297 is the determined cDNA sequence for clone 25356.
SEQ ID NO:298 is the determined cDNA sequence for clone 25357.
SEQ ID NO:299 is the determined cDNA sequence for clone 25361.
SEQ ID NO:300 is the determined cDNA sequence for clone 25363.
- 10 SEQ ID NO:301 is the determined cDNA sequence for clone 25397.
SEQ ID NO:302 is the determined cDNA sequence for clone 25402.
SEQ ID NO:303 is the determined cDNA sequence for clone 25403.
SEQ ID NO:304 is the determined cDNA sequence for clone 25405.
SEQ ID NO:305 is the determined cDNA sequence for clone 25407.
- 15 SEQ ID NO:306 is the determined cDNA sequence for clone 25409.
SEQ ID NO:307 is the determined cDNA sequence for clone 25396.
SEQ ID NO:308 is the determined cDNA sequence for clone 25414.
SEQ ID NO:309 is the determined cDNA sequence for clone 25410.
SEQ ID NO:310 is the determined cDNA sequence for clone 25406.
- 20 SEQ ID NO:311 is the determined cDNA sequence for clone 25306.
SEQ ID NO:312 is the determined cDNA sequence for clone 25362.
SEQ ID NO:313 is the determined cDNA sequence for clone 25360.
SEQ ID NO:314 is the determined cDNA sequence for clone 25398.
SEQ ID NO:315 is the determined cDNA sequence for clone 25355.
- 25 SEQ ID NO:316 is the determined cDNA sequence for clone 25351.
SEQ ID NO:317 is the determined cDNA sequence for clone 25331.
SEQ ID NO:318 is the determined cDNA sequence for clone 25338.
SEQ ID NO:319 is the determined cDNA sequence for clone 25335.
SEQ ID NO:320 is the determined cDNA sequence for clone 25329.
- 30 SEQ ID NO:321 is the determined cDNA sequence for clone 25324.
SEQ ID NO:322 is the determined cDNA sequence for clone 25322.

- SEQ ID NO:323 is the determined cDNA sequence for clone 25319.
SEQ ID NO:324 is the determined cDNA sequence for clone 25316.
SEQ ID NO:325 is the determined cDNA sequence for clone 25311.
SEQ ID NO:326 is the determined cDNA sequence for clone 25310.
5 SEQ ID NO:327 is the determined cDNA sequence for clone 25302.
SEQ ID NO:328 is the determined cDNA sequence for clone 25315.
SEQ ID NO:329 is the determined cDNA sequence for clone 25308.
SEQ ID NO:330 is the determined cDNA sequence for clone 25303.
SEQ ID NO:331-337 are the cDNA sequences of isoforms of the p53 tumor suppressor
10 homologue, p63 (also referred to as L530S).
SEQ ID NO:338-344 are the amino acid sequences encoded by SEQ ID NO:331-337,
respectively
SEQ ID NO:345 is a second cDNA sequence for the antigen L763P.
SEQ ID NO:346 is the amino acid sequence encoded by the sequence of SEQ ID NO:
15 345.
SEQ ID NO:347 is a determined full-length cDNA sequence for L523S.
SEQ ID NO:348 is the amino acid sequence encoded by SEQ ID NO: 347.
SEQ ID NO:349 is the cDNA sequence encoding the N-terminal portion of L773P.
SEQ ID NO:350 is the amino acid sequence of the N-terminal portion of L773P.
20 SEQ ID NO:351 is the DNA sequence for a fusion of Ra12 and the N-terminal portion
of L763P.
SEQ ID NO:352 is the amino acid sequence of the fusion of Ra12 and the N-terminal
portion of L763P.
SEQ ID NO:353 is the DNA sequence for a fusion of Ra12 and the C-terminal portion
25 of L763P.
SEQ ID NO:354 is the amino acid sequence of the fusion of Ra12 and the C-terminal
portion of L763P.
SEQ ID NO:355 is a primer.
SEQ ID NO:356 is a primer.
30 SEQ ID NO:357 is the protein sequence of expressed recombinant L762P.
SEQ ID NO:358 is the DNA sequence of expressed recombinant L762P.

- SEQ ID NO:359 is a primer.
- SEQ ID NO:360 is a primer.
- SEQ ID NO:361 is the protein sequence of expressed recombinant L773P A.
- SEQ ID NO:362 is the DNA sequence of expressed recombinant L773P A.
- 5 SEQ ID NO:363 is an epitope derived from clone L773P polypeptide.
- SEQ ID NO:364 is a polynucleotide encoding the polypeptide of SEQ ID NO:363.
- SEQ ID NO:365 is an epitope derived from clone L773P polypeptide.
- SEQ ID NO:366 is a polynucleotide encoding the polypeptide of SEQ ID NO:365.
- SEQ ID NO:367 is an epitope consisting of amino acids 571-590 of SEQ ID NO:161,
- 10 clone L762P.
- SEQ ID NO:368 is the full-length DNA sequence for contig 13 (SEQ ID NO:125), also referred to as L761P.
- SEQ ID NO:369 is the protein sequence encoded by the DNA sequence of SEQ ID NO:368.
- 15 SEQ ID NO:370 is an L762P DNA sequence from nucleotides 2071-2130.
- SEQ ID NO:371 is an L762P DNA sequence from nucleotides 1441-1500.
- SEQ ID NO:372 is an L762P DNA sequence from nucleotides 1936-1955.
- SEQ ID NO:373 is an L762P DNA sequence from nucleotides 2620-2679.
- SEQ ID NO:374 is an L762P DNA sequence from nucleotides 1801-1860.
- 20 SEQ ID NO:375 is an L762P DNA sequence from nucleotides 1531-1591.
- SEQ ID NO:376 is the amino acid sequence of the L762P peptide encoded by SEQ ID NO:373.
- SEQ ID NO:377 is the amino acid sequence of the L762P peptide encoded by SEQ ID NO:370.
- 25 SEQ ID NO:378 is the amino acid sequence of the L762P peptide encoded by SEQ ID NO:372.
- SEQ ID NO:379 is the amino acid sequence of the L762P peptide encoded by SEQ ID NO:374.
- SEQ ID NO:380 is the amino acid sequence of the L762P peptide encoded by SEQ ID
- 30 NO:371.

- SEQ ID NO:381 is the amino acid sequence of the L762P peptide encoded by SEQ ID NO:375.
- SEQ ID NO:382 is the amino acid sequence of an epitope of L762P.
- SEQ ID NO:383-386 are PCR primers.
- 5 SEQ ID NO:387-395 are the amino acid sequences of L773P peptides.
- SEQ ID NO:396-419 are the amino acid sequences of L523S peptides.
- SEQ ID NO:420 is the determined cDNA sequence for clone #19014.
- SEQ ID NO:421 is the forward primer PDM-278 for the L514S-13160 coding region.
- SEQ ID NO:422 is the reverse primer PDM-278 for the L514S-13160 coding region.
- 10 SEQ ID NO:423 is the amino acid sequence for the expressed recombinant L514S.
- SEQ ID NO:424 is the DNA coding sequence for the recombinant L514S.
- SEQ ID NO:425 is the forward primer PDM-414 for the L523S coding region.
- SEQ ID NO:426 is the reverse primer PDM-414 for the L523S coding region.
- SEQ ID NO:427 is the amino acid sequence for the expressed recombinant L523S.
- 15 SEQ ID NO:428 is the DNA coding sequence for the recombinant L523S.
- SEQ ID NO:429 is the reverse primer PDM-279 for the L762PA coding region.
- SEQ ID NO:430 is the amino acid sequence for the expressed recombinant L762PA.
- SEQ ID NO:431 is the DNA coding sequence for the recombinant L762PA.
- SEQ ID NO:432 is the reverse primer PDM-300 for the L773P coding region.
- 20 SEQ ID NO:433 is the amino acid sequence of the expressed recombinant L773P.
- SEQ ID NO:434 is the DNA coding sequence for the recombinant L773P.
- SEQ ID NO:435 is the forward primer for TCR Valpha8.
- SEQ ID NO:436 is the reverse primer for TCR Valpha8.
- SEQ ID NO:437 is the forward primer for TCR Vbeta8.
- 25 SEQ ID NO:438 is the reverse primer for TCR Vbeta8.
- SEQ ID NO:439 is the TCR Valpha DNA sequence of the TCR clone specific for the lung antigen L762P.
- SEQ ID NO:440 is the TCR Vbeta DNA sequence of the TCR clone specific for the lung antigen L762P.
- 30 SEQ ID NO:441 is the amino acid sequence of L763 peptide #2684.

- SEQ ID NO:442 is the predicted full-length cDNA for the cloned partial sequence of clone L529S (SEQ ID NO:106).
- SEQ ID NO:443 is the deduced amino acid sequence encoded by SEQ ID NO:442.
- SEQ ID NO:444 is the forward primer PDM-734 for the coding region of clone L523S.
- 5 SEQ ID NO:445 is the reverse primer PDM-735 for the coding region of clone L523S.
- SEQ ID NO:446 is the amino acid sequence for the expressed recombinant L523S.
- SEQ ID NO:447 is the DNA coding sequence for the recombinant L523S.
- SEQ ID NO:448 is another forward primer PDM-733 for the coding region of clone L523S.
- 10 SEQ ID NO:449 is the amino acid sequence for a second expressed recombinant L523S.
- SEQ ID NO:450 is the DNA coding sequence for a second recombinant L523S.
- SEQ ID NO:451 corresponds to amino acids 86-110, an epitope of L514S-specific in the generation of antibodies.
- SEQ ID NO:452 corresponds to amino acids 21-45, an epitope of L514S-specific in the
- 15 generation of antibodies.
- SEQ ID NO:453 corresponds to amino acids 121-135, an epitope of L514S-specific in the generation of antibodies.
- SEQ ID NO:454 corresponds to amino acids 440-460, an epitope of L523S-specific in the generation of antibodies.
- 20 SEQ ID NO:455 corresponds to amino acids 156-175, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:456 corresponds to amino acids 326-345, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:457 corresponds to amino acids 40-59, an epitope of L523S-specific in the
- 25 generation of antibodies.
- SEQ ID NO:458 corresponds to amino acids 80-99, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:459 corresponds to amino acids 160-179, an epitope of L523S-specific in the generation of antibodies.
- 30 SEQ ID NO:460 corresponds to amino acids 180-199, an epitope of L523S-specific in the generation of antibodies.

- SEQ ID NO:461 corresponds to amino acids 320-339, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:462 corresponds to amino acids 340-359, an epitope of L523S-specific in the generation of antibodies.
- 5 SEQ ID NO:463 corresponds to amino acids 370-389, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:464 corresponds to amino acids 380-399, an epitope of L523S-specific in the generation of antibodies.
- SEQ ID NO:465 corresponds to amino acids 37-55, an epitope of L523S-recognized by the L523S-specific CTL line 6B1.
- 10 SEQ ID NO:466 corresponds to amino acids 41-51, the mapped antigenic epitope of L523S-recognized by the L523S-specific CTL line 6B1.
- SEQ ID NO:467 corresponds to the DNA sequence which encodes SEQ ID NO:466.
- SEQ ID NO:468 corresponds to the amino acids of peptide 16, 17 of hL523S.
- 15 SEQ ID NO:469 corresponds to the amino acids of peptide 16, 17 of mL523S

DETAILED DESCRIPTION OF THE INVENTION

The present invention is directed generally to compositions and their use in the therapy and diagnosis of cancer, particularly lung cancer. As described further below, illustrative compositions of the present invention include, but are not restricted to, polypeptides, particularly immunogenic polypeptides, polynucleotides encoding such polypeptides, antibodies and other binding agents, antigen presenting cells (APCs) and immune system cells (*e.g.*, T cells).

20

The practice of the present invention will employ, unless indicated specifically to the contrary, conventional methods of virology, immunology, microbiology, molecular biology and recombinant DNA techniques within the skill of the art, many of which are described below for the purpose of illustration. Such techniques are explained fully in the literature. See, *e.g.*, Sambrook, et al. *Molecular Cloning: A Laboratory Manual* (2nd Edition, 1989); Maniatis et al. *Molecular Cloning: A Laboratory Manual* (1982); DNA Cloning: A Practical Approach, vol. I & II (D. Glover, ed.); *Oligonucleotide Synthesis* (N. Gait, ed., 1984); *Nucleic Acid*

25

30

Hybridization (B. Hames & S. Higgins, eds., 1985); Transcription and Translation (B. Hames & S. Higgins, eds., 1984); Animal Cell Culture (R. Freshney, ed., 1986); Perbal, A Practical Guide to Molecular Cloning (1984).

All publications, patents and patent applications cited herein, whether
5 supra or infra, are hereby incorporated by reference in their entirety.

As used in this specification and the appended claims, the singular forms
"a," "an" and "the" include plural references unless the content clearly dictates
otherwise.

Polypeptide Compositions

10 As used herein, the term "polypeptide" " is used in its conventional
meaning, *i.e.*, as a sequence of amino acids. The polypeptides are not limited to a
specific length of the product; thus, peptides, oligopeptides, and proteins are included
within the definition of polypeptide, and such terms may be used interchangeably herein
unless specifically indicated otherwise. This term also does not refer to or exclude post-
15 expression modifications of the polypeptide, for example, glycosylations, acetylations,
phosphorylations and the like, as well as other modifications known in the art, both
naturally occurring and non-naturally occurring. A polypeptide may be an entire
protein, or a subsequence thereof. Particular polypeptides of interest in the context of
this invention are amino acid subsequences comprising epitopes, *i.e.*, antigenic
20 determinants substantially responsible for the immunogenic properties of a polypeptide
and being capable of evoking an immune response.

Particularly illustrative polypeptides of the present invention comprise
those encoded by a polynucleotide sequence set forth in any one of SEQ ID NO:1-3, 6-
8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-
25 82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153,
154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209,
210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375,
420, 424, 428, 431, 434, 442, 447, 450 and 467, or a sequence that hybridizes under
moderately stringent conditions, or, alternatively, under highly stringent conditions, to a
30 polynucleotide sequence set forth in any one of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29,

30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 5 431, 434, 442, 447, 450 and 467. Certain illustrative polypeptides of the invention comprise amino acid sequences as set forth in any one of SEQ ID NO:152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344, 346, 350, 357, 361, 363, 365, 367, 369, 376-382, 387-419, 423, 427, 430, 433, 441, 443, 446, 449, 451-466 and 468-469.

10 The polypeptides of the present invention are sometimes herein referred to as lung tumor proteins or lung tumor polypeptides, as an indication that their identification has been based at least in part upon their increased levels of expression in lung tumor samples. Thus, a "lung tumor polypeptide" or "lung tumor protein," refers generally to a polypeptide sequence of the present invention, or a polynucleotide 15 sequence encoding such a polypeptide, that is expressed in a substantial proportion of lung tumor samples, for example preferably greater than about 20%, more preferably greater than about 30%, and most preferably greater than about 50% or more of lung tumor samples tested, at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in normal tissues, as determined using a 20 representative assay provided herein. A lung tumor polypeptide sequence of the invention, based upon its increased level of expression in tumor cells, has particular utility both as a diagnostic marker as well as a therapeutic target, as further described below.

 In certain preferred embodiments, the polypeptides of the invention are 25 immunogenic, *i.e.*, they react detectably within an immunoassay (such as an ELISA or T-cell stimulation assay) with antisera and/or T-cells from a patient with lung cancer. Screening for immunogenic activity can be performed using techniques well known to the skilled artisan. For example, such screens can be performed using methods such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring 30 Harbor Laboratory, 1988. In one illustrative example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of

antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ¹²⁵I-labeled Protein A.

As would be recognized by the skilled artisan, immunogenic portions of the polypeptides disclosed herein are also encompassed by the present invention. An
5 "immunogenic portion," as used herein, is a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive (*i.e.*, specifically binds) with the B-cells and/or T-cell surface antigen receptors that recognize the polypeptide. Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press,
10 1993) and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (*i.e.*, they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and
15 antibodies may be prepared as described herein, and using well-known techniques.

In one preferred embodiment, an immunogenic portion of a polypeptide of the present invention is a portion that reacts with antisera and/or T-cells at a level that is not substantially less than the reactivity of the full-length polypeptide (*e.g.*, in an ELISA and/or T-cell reactivity assay). Preferably, the level of immunogenic activity of
20 the immunogenic portion is at least about 50%, preferably at least about 70% and most preferably greater than about 90% of the immunogenicity for the full-length polypeptide. In some instances, preferred immunogenic portions will be identified that have a level of immunogenic activity greater than that of the corresponding full-length polypeptide, *e.g.*, having greater than about 100% or 150% or more immunogenic
25 activity.

In certain other embodiments, illustrative immunogenic portions may include peptides in which an N-terminal leader sequence and/or transmembrane domain have been deleted. Other illustrative immunogenic portions will contain a small N- and/or C-terminal deletion (*e.g.*, 1-30 amino acids, preferably 5-15 amino acids),
30 relative to the mature protein.

In another embodiment, a polypeptide composition of the invention may also comprise one or more polypeptides that are immunologically reactive with T cells and/or antibodies generated against a polypeptide of the invention, particularly a polypeptide having an amino acid sequence disclosed herein, or to an immunogenic
5 fragment or variant thereof.

In another embodiment of the invention, polypeptides are provided that comprise one or more polypeptides that are capable of eliciting T cells and/or antibodies that are immunologically reactive with one or more polypeptides described herein, or one or more polypeptides encoded by contiguous nucleic acid sequences contained in
10 the polynucleotide sequences disclosed herein, or immunogenic fragments or variants thereof, or to one or more nucleic acid sequences which hybridize to one or more of these sequences under conditions of moderate to high stringency.

The present invention, in another aspect, provides polypeptide fragments comprising at least about 5, 10, 15, 20, 25, 50, or 100 contiguous amino acids, or more,
15 including all intermediate lengths, of a polypeptide compositions set forth herein, such as those set forth in SEQ ID NO:152, 155, 156, 165, 166, 169, 170, 172, 174, 176, 226-252, 338-344, 346, 350, 357, 361, 363, 365, 367, 369, 376-382 and 387-419, 441, 443, 446, 449, 451-466 and 468-469, or those encoded by a polynucleotide sequence set forth in a sequence of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54,
20 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467.

In another aspect, the present invention provides variants of the polypeptide compositions described herein. Polypeptide variants generally encompassed by the present invention will typically exhibit at least about 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% or more identity (determined as described below), along its length, to a polypeptide sequences set forth
30 herein.

In one preferred embodiment, the polypeptide fragments and variants provide by the present invention are immunologically reactive with an antibody and/or T-cell that reacts with a full-length polypeptide specifically set for the herein.

In another preferred embodiment, the polypeptide fragments and variants
5 provided by the present invention exhibit a level of immunogenic activity of at least about 50%, preferably at least about 70%, and most preferably at least about 90% or more of that exhibited by a full-length polypeptide sequence specifically set forth herein.

A polypeptide "variant," as the term is used herein, is a polypeptide that
10 typically differs from a polypeptide specifically disclosed herein in one or more substitutions, deletions, additions and/or insertions. Such variants may be naturally occurring or may be synthetically generated, for example, by modifying one or more of the above polypeptide sequences of the invention and evaluating their immunogenic activity as described herein and/or using any of a number of techniques well known in
15 the art.

For example, certain illustrative variants of the polypeptides of the invention include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other illustrative variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino
20 acids) has been removed from the N- and/or C-terminal of the mature protein.

In many instances, a variant will contain conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure and hydropathic nature of the
25 polypeptide to be substantially unchanged. As described above, modifications may be made in the structure of the polynucleotides and polypeptides of the present invention and still obtain a functional molecule that encodes a variant or derivative polypeptide with desirable characteristics, e.g., with immunogenic characteristics. When it is desired to alter the amino acid sequence of a polypeptide to create an equivalent, or
30 even an improved, immunogenic variant or portion of a polypeptide of the invention,

one skilled in the art will typically change one or more of the codons of the encoding DNA sequence according to Table 1.

For example, certain amino acids may be substituted for other amino acids in a protein structure without appreciable loss of interactive binding capacity with structures such as, for example, antigen-binding regions of antibodies or binding sites on substrate molecules. Since it is the interactive capacity and nature of a protein that defines that protein's biological functional activity, certain amino acid sequence substitutions can be made in a protein sequence, and, of course, its underlying DNA coding sequence, and nevertheless obtain a protein with like properties. It is thus contemplated that various changes may be made in the peptide sequences of the disclosed compositions, or corresponding DNA sequences which encode said peptides without appreciable loss of their biological utility or activity.

Table 1

Amino Acids			Codons						
Alanine	Ala	A	GCA	GCC	GCG	GCU			
Cysteine	Cys	C	UGC	UGU					
Aspartic acid	Asp	D	GAC	GAU					
Glutamic acid	Glu	E	GAA	GAG					
Phenylalanine	Phe	F	UUC	UUU					
Glycine	Gly	G	GGA	GGC	GGG	GGU			
Histidine	His	H	CAC	CAU					
Isoleucine	Ile	I	AUA	AUC	AUU				
Lysine	Lys	K	AAA	AAG					
Leucine	Leu	L	UUA	UUG	CUA	CUC	CUG	CUU	
Methionine	Met	M	AUG						
Asparagine	Asn	N	AAC	AAU					
Proline	Pro	P	CCA	CCC	CCG	CCU			
Glutamine	Gln	Q	CAA	CAG					
Arginine	Arg	R	AGA	AGG	CGA	CGC	CGG	CGU	
Serine	Ser	S	AGC	AGU	UCA	UCC	UCG	UCU	
Threonine	Thr	T	ACA	ACC	ACG	ACU			
Valine	Val	V	GUA	GUC	GUG	GUU			
Tryptophan	Trp	W	UGG						
Tyrosine	Tyr	Y	UAC	UAU					

In making such changes, the hydropathic index of amino acids may be considered. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference). It is accepted that the relative hydropathic character of the amino acid contributes to the secondary structure of the resultant protein, which in turn defines the interaction of the protein with other molecules, for example, enzymes, substrates, receptors, DNA, antibodies, antigens, and the like. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are:

isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (−0.4); threonine (−0.7); serine (−0.8); tryptophan (−0.9); tyrosine (−1.3); proline (−1.6); histidine (−3.2); glutamate (−3.5); glutamine (−3.5); aspartate (−3.5); asparagine (−3.5); lysine (−3.9); and arginine (−4.5).

5 It is known in the art that certain amino acids may be substituted by other amino acids having a similar hydropathic index or score and still result in a protein with similar biological activity, *i.e.* still obtain a biological functionally equivalent protein. In making such changes, the substitution of amino acids whose hydropathic indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity. U. S. Patent 4,554,101 (specifically incorporated herein by reference in its entirety), states that the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with a biological property of the protein.

15 As detailed in U. S. Patent 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 \pm 1); glutamate (+3.0 \pm 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (−0.4); proline (−0.5 \pm 1); alanine (−0.5); histidine (−0.5); cysteine (−1.0); methionine (−1.3); valine (−1.5); leucine (−1.8); isoleucine (−1.8); tyrosine (−2.3); phenylalanine (−2.5); tryptophan (−3.4). It is understood that an amino acid can be substituted for another having a similar hydrophilicity value and still obtain a biologically equivalent, and in particular, an immunologically equivalent protein. In such changes, the substitution of amino acids whose hydrophilicity values are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

25 As outlined above, amino acid substitutions are generally therefore based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. Exemplary substitutions that take various of the foregoing characteristics into consideration are well known to those of skill in the art and include: arginine and lysine; glutamate and aspartate; serine and threonine; glutamine and asparagine; and valine, leucine and isoleucine.

In addition, any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3' ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl-methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

Amino acid substitutions may further be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain non-conservative changes. In a preferred embodiment, variant polypeptides differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein, which co-translationally or post-translationally directs transfer of the protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

When comparing polypeptide sequences, two sequences are said to be "identical" if the sequence of amino acids in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two

sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA* 80:726-730.

Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402

and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides and polypeptides of the invention. Software for performing BLAST analyses is publicly available through the National Center for
5 Biotechnology Information. For amino acid sequences, a scoring matrix can be used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is
10 reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment.

In one preferred approach, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polypeptide sequence in
15 the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of
20 matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described herein, or that comprises
25 at least one polypeptide as described herein and an unrelated sequence, such as a known tumor protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner), preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological
30 and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the polypeptide or to enable the polypeptide to be targeted to

desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the polypeptide.

Fusion polypeptides may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion polypeptide is expressed as a recombinant polypeptide, allowing the production of increased levels, relative to a non-fused polypeptide, in an expression system. Briefly, DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion polypeptide that retains the biological activity of both component polypeptides.

A peptide linker sequence may be employed to separate the first and second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion polypeptide using standard techniques well known in the art. Suitable peptide linker sequences may be chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements

responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

5 The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein, such as an immunogenic protein capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (*see, for example, Stoute et al. New Engl. J. Med., 336:86-91, 1997*).

10 In one preferred embodiment, the immunological fusion partner is derived from a *Mycobacterium* sp., such as a *Mycobacterium tuberculosis*-derived Ra12 fragment. Ra12 compositions and methods for their use in enhancing the expression and/or immunogenicity of heterologous polynucleotide/polypeptide sequences is described in U.S. Patent Application 60/158,585, the disclosure of which is
15 incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application
20 60/158,585; *see also, Skeiky et al., Infection and Immun. (1999) 67:3998-4007*, incorporated herein by reference). C-terminal fragments of the MTB32A coding sequence express at high levels and remain as a soluble polypeptides throughout the purification process. Moreover, Ra12 may enhance the immunogenicity of heterologous immunogenic polypeptides with which it is fused. One preferred Ra12 fusion
25 polypeptide comprises a 14 KD C-terminal fragment corresponding to amino acid residues 192 to 323 of MTB32A.

 Other preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300
30 nucleotides that encode a portion of a Ra12 polypeptide.

Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Within other preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium *Haemophilus influenza B* (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemagglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the *LytA* gene; *Gene* 43:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (*see Biotechnology* 10:795-798,

1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion polypeptide. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

Yet another illustrative embodiment involves fusion polypeptides, and
5 the polynucleotides encoding them, wherein the fusion partner comprises a targeting signal capable of directing a polypeptide to the endosomal/lysosomal compartment, as described in U.S. Patent No. 5,633,234. An immunogenic polypeptide of the invention, when fused with this targeting signal, will associate more efficiently with MHC class II molecules and thereby provide enhanced in vivo stimulation of CD4⁺ T-cells specific
10 for the polypeptide.

Polypeptides of the invention are prepared using any of a variety of well known synthetic and/or recombinant techniques, the latter of which are further described below. Polypeptides, portions and other variants generally less than about 150 amino acids can be generated by synthetic means, using techniques well known to
15 those of ordinary skill in the art. In one illustrative example, such polypeptides are synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase synthesis method, where amino acids are sequentially added to a growing amino acid chain. See Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from
20 suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

In general, polypeptide compositions (including fusion polypeptides) of the invention are isolated. An "isolated" polypeptide is one that is removed from its original environment. For example, a naturally-occurring protein or polypeptide is
25 isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are also purified, e.g., are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure.

Polynucleotide Compositions

30 The present invention, in other aspects, provides polynucleotide compositions. The terms "DNA" and "polynucleotide" are used essentially

interchangeably herein to refer to a DNA molecule that has been isolated free of total genomic DNA of a particular species. "Isolated," as used herein, means that a polynucleotide is substantially away from other coding sequences, and that the DNA molecule does not contain large portions of unrelated coding DNA, such as large
5 chromosomal fragments or other functional genes or polypeptide coding regions. Of course, this refers to the DNA molecule as originally isolated, and does not exclude genes or coding regions later added to the segment by the hand of man.

As will be understood by those skilled in the art, the polynucleotide compositions of this invention can include genomic sequences, extra-genomic and
10 plasmid-encoded sequences and smaller engineered gene segments that express, or may be adapted to express, proteins, polypeptides, peptides and the like. Such segments may be naturally isolated, or modified synthetically by the hand of man.

As will be also recognized by the skilled artisan, polynucleotides of the invention may be single-stranded (coding or antisense) or double-stranded, and may be
15 DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules may include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules
20 and/or support materials.

Polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a polypeptide/protein of the invention or a portion thereof) or may comprise a sequence that encodes a variant or derivative, preferably and immunogenic variant or derivative, of such a sequence.

Therefore, according to another aspect of the present invention, polynucleotide compositions are provided that comprise some or all of a polynucleotide sequence set forth in any one of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49,
51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113,
125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168,
30 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224,
253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434,

442, 447, 450 and 467, complements of a polynucleotide sequence set forth in any one of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467, and degenerate variants of a polynucleotide sequence set forth in any one of SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467. In certain preferred embodiments, the polynucleotide sequences set forth herein encode immunogenic polypeptides, as described above.

In other related embodiments, the present invention provides polynucleotide variants having substantial identity to the sequences disclosed herein in SEQ ID NO:1-3, 6-8, 10-13, 15-27, 29, 30, 32, 34-49, 51, 52, 54, 55, 57-59, 61-69, 71, 73, 74, 77, 78, 80-82, 84, 86-96, 107-109, 111, 113, 125, 127, 128, 129, 131-133, 142, 144, 148-151, 153, 154, 157, 158, 160, 167, 168, 171, 179, 182, 184-186, 188-191, 193, 194, 198-207, 209, 210, 213, 214, 217, 220-224, 253-337, 345, 347, 349, 358, 362, 364, 365, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467, for example those comprising at least 70% sequence identity, preferably at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% or higher, sequence identity compared to a polynucleotide sequence of this invention using the methods described herein, (e.g., BLAST analysis using standard parameters, as described below). One skilled in this art will recognize that these values can be appropriately adjusted to determine corresponding identity of proteins encoded by two nucleotide sequences by taking into account codon degeneracy, amino acid similarity, reading frame positioning and the like.

Typically, polynucleotide variants will contain one or more substitutions, additions, deletions and/or insertions, preferably such that the immunogenicity of the

polypeptide encoded by the variant polynucleotide is not substantially diminished relative to a polypeptide encoded by a polynucleotide sequence specifically set forth herein). The term "variants" should also be understood to encompass homologous genes of xenogenic origin.

5 In additional embodiments, the present invention provides polynucleotide fragments comprising various lengths of contiguous stretches of sequence identical to or complementary to one or more of the sequences disclosed herein. For example, polynucleotides are provided by this invention that comprise at least about 10, 15, 20, 30, 40, 50, 75, 100, 150, 200, 300, 400, 500 or 1000 or more
10 contiguous nucleotides of one or more of the sequences disclosed herein as well as all intermediate lengths there between. It will be readily understood that "intermediate lengths", in this context, means any length between the quoted values, such as 16, 17, 18, 19, *etc.*; 21, 22, 23, *etc.*; 30, 31, 32, *etc.*; 50, 51, 52, 53, *etc.*; 100, 101, 102, 103, *etc.*; 150, 151, 152, 153, *etc.*; including all integers through 200-500; 500-1,000, and the
15 like.

 In another embodiment of the invention, polynucleotide compositions are provided that are capable of hybridizing under moderate to high stringency conditions to a polynucleotide sequence provided herein, or a fragment thereof, or a complementary sequence thereof. Hybridization techniques are well known in the art of molecular
20 biology. For purposes of illustration, suitable moderately stringent conditions for testing the hybridization of a polynucleotide of this invention with other polynucleotides include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-60°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. One skilled in
25 the art will understand that the stringency of hybridization can be readily manipulated, such as by altering the salt content of the hybridization solution and/or the temperature at which the hybridization is performed. For example, in another embodiment, suitable highly stringent hybridization conditions include those described above, with the exception that the temperature of hybridization is increased, *e.g.*, to 60-65°C or 65-
30 70°C.

In certain preferred embodiments, the polynucleotides described above, e.g., polynucleotide variants, fragments and hybridizing sequences, encode polypeptides that are immunologically cross-reactive with a polypeptide sequence specifically set forth herein. In other preferred embodiments, such polynucleotides encode
5 polypeptides that have a level of immunogenic activity of at least about 50%, preferably at least about 70%, and more preferably at least about 90% of that for a polypeptide sequence specifically set forth herein.

The polynucleotides of the present invention, or fragments thereof, regardless of the length of the coding sequence itself, may be combined with other DNA
10 sequences, such as promoters, polyadenylation signals, additional restriction enzyme sites, multiple cloning sites, other coding segments, and the like, such that their overall length may vary considerably. It is therefore contemplated that a nucleic acid fragment of almost any length may be employed, with the total length preferably being limited by the ease of preparation and use in the intended recombinant DNA protocol. For
15 example, illustrative polynucleotide segments with total lengths of about 10,000, about 5000, about 3000, about 2,000, about 1,000, about 500, about 200, about 100, about 50 base pairs in length, and the like, (including all intermediate lengths) are contemplated to be useful in many implementations of this invention.

When comparing polynucleotide sequences, two sequences are said to be
20 "identical" if the sequence of nucleotides in the two sequences is the same when aligned for maximum correspondence, as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions,
25 usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR,
30 Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A

- model of evolutionary change in proteins – Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) *Atlas of Protein Sequence and Structure*, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) *Unified Approach to Alignment and Phylogenies* pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad. Sci. USA* 80:726-730.

- Alternatively, optimal alignment of sequences for comparison may be conducted by the local identity algorithm of Smith and Waterman (1981) *Add. APL. Math* 2:482, by the identity alignment algorithm of Needleman and Wunsch (1970) *J. Mol. Biol.* 48:443, by the search for similarity methods of Pearson and Lipman (1988) *Proc. Natl. Acad. Sci. USA* 85: 2444, by computerized implementations of these algorithms (GAP, BESTFIT, BLAST, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group (GCG), 575 Science Dr., Madison, WI), or by inspection.

- One preferred example of algorithms that are suitable for determining percent sequence identity and sequence similarity are the BLAST and BLAST 2.0 algorithms, which are described in Altschul et al. (1977) *Nucl. Acids Res.* 25:3389-3402 and Altschul et al. (1990) *J. Mol. Biol.* 215:403-410, respectively. BLAST and BLAST 2.0 can be used, for example with the parameters described herein, to determine percent sequence identity for the polynucleotides of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information. In one illustrative example, cumulative scores can be calculated using, for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always >0) and N (penalty score for mismatching residues; always <0). Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments;

or the end of either sequence is reached. The BLAST algorithm parameters W, T and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) *Proc. Natl. Acad. Sci. USA* 89:10915) alignments, (B) of 50, expectation (E) of 10, M=5, N=-4 and a comparison of both strands.

Preferably, the "percentage of sequence identity" is determined by comparing two optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide sequence in the comparison window may comprise additions or deletions (*i.e.*, gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of positions at which the identical nucleic acid bases occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.*, the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Therefore, in another embodiment of the invention, a mutagenesis approach, such as site-specific mutagenesis, is employed for the preparation of immunogenic variants and/or derivatives of the polypeptides described herein. By this

approach, specific modifications in a polypeptide sequence can be made through mutagenesis of the underlying polynucleotides that encode them. These techniques provides a straightforward approach to prepare and test sequence variants, for example, incorporating one or more of the foregoing considerations, by introducing one or more
5 nucleotide sequence changes into the polynucleotide.

Site-specific mutagenesis allows the production of mutants through the use of specific oligonucleotide sequences which encode the DNA sequence of the desired mutation, as well as a sufficient number of adjacent nucleotides, to provide a primer sequence of sufficient size and sequence complexity to form a stable duplex on
10 both sides of the deletion junction being traversed. Mutations may be employed in a selected polynucleotide sequence to improve, alter, decrease, modify, or otherwise change the properties of the polynucleotide itself, and/or alter the properties, activity, composition, stability, or primary sequence of the encoded polypeptide.

In certain embodiments of the present invention, the inventors
15 contemplate the mutagenesis of the disclosed polynucleotide sequences to alter one or more properties of the encoded polypeptide, such as the immunogenicity of a polypeptide vaccine. The techniques of site-specific mutagenesis are well-known in the art, and are widely used to create variants of both polypeptides and polynucleotides. For example, site-specific mutagenesis is often used to alter a specific portion of a DNA
20 molecule. In such embodiments, a primer comprising typically about 14 to about 25 nucleotides or so in length is employed, with about 5 to about 10 residues on both sides of the junction of the sequence being altered.

As will be appreciated by those of skill in the art, site-specific mutagenesis techniques have often employed a phage vector that exists in both a single
25 stranded and double stranded form. Typical vectors useful in site-directed mutagenesis include vectors such as the M13 phage. These phage are readily commercially-available and their use is generally well-known to those skilled in the art. Double-stranded plasmids are also routinely employed in site directed mutagenesis that eliminates the step of transferring the gene of interest from a plasmid to a phage.

30 In general, site-directed mutagenesis in accordance herewith is performed by first obtaining a single-stranded vector or melting apart of two strands of a

double-stranded vector that includes within its sequence a DNA sequence that encodes the desired peptide. An oligonucleotide primer bearing the desired mutated sequence is prepared, generally synthetically. This primer is then annealed with the single-stranded vector, and subjected to DNA polymerizing enzymes such as *E. coli* polymerase I
5 Klenow fragment, in order to complete the synthesis of the mutation-bearing strand. Thus, a heteroduplex is formed wherein one strand encodes the original non-mutated sequence and the second strand bears the desired mutation. This heteroduplex vector is then used to transform appropriate cells, such as *E. coli* cells, and clones are selected which include recombinant vectors bearing the mutated sequence arrangement.

10 The preparation of sequence variants of the selected peptide-encoding DNA segments using site-directed mutagenesis provides a means of producing potentially useful species and is not meant to be limiting as there are other ways in which sequence variants of peptides and the DNA sequences encoding them may be obtained. For example, recombinant vectors encoding the desired peptide sequence
15 may be treated with mutagenic agents, such as hydroxylamine, to obtain sequence variants. Specific details regarding these methods and protocols are found in the teachings of Maloy *et al.*, 1994; Segal, 1976; Prokop and Bajpai, 1991; Kuby, 1994; and Maniatis *et al.*, 1982, each incorporated herein by reference, for that purpose.

As used herein, the term "oligonucleotide directed mutagenesis
20 procedure" refers to template-dependent processes and vector-mediated propagation which result in an increase in the concentration of a specific nucleic acid molecule relative to its initial concentration, or in an increase in the concentration of a detectable signal, such as amplification. As used herein, the term "oligonucleotide directed mutagenesis procedure" is intended to refer to a process that involves the
25 template-dependent extension of a primer molecule. The term template dependent process refers to nucleic acid synthesis of an RNA or a DNA molecule wherein the sequence of the newly synthesized strand of nucleic acid is dictated by the well-known rules of complementary base pairing (see, for example, Watson, 1987). Typically, vector mediated methodologies involve the introduction of the nucleic acid fragment
30 into a DNA or RNA vector, the clonal amplification of the vector, and the recovery of

the amplified nucleic acid fragment. Examples of such methodologies are provided by U. S. Patent No. 4,237,224, specifically incorporated herein by reference in its entirety.

In another approach for the production of polypeptide variants of the present invention, recursive sequence recombination, as described in U.S. Patent No. 5,837,458, may be employed. In this approach, iterative cycles of recombination and screening or selection are performed to "evolve" individual polynucleotide variants of the invention having, for example, enhanced immunogenic activity.

In other embodiments of the present invention, the polynucleotide sequences provided herein can be advantageously used as probes or primers for nucleic acid hybridization. As such, it is contemplated that nucleic acid segments that comprise a sequence region of at least about 15 nucleotide long contiguous sequence that has the same sequence as, or is complementary to, a 15 nucleotide long contiguous sequence disclosed herein will find particular utility. Longer contiguous identical or complementary sequences, *e.g.*, those of about 20, 30, 40, 50, 100, 200, 500, 1000 (including all intermediate lengths) and even up to full length sequences will also be of use in certain embodiments.

The ability of such nucleic acid probes to specifically hybridize to a sequence of interest will enable them to be of use in detecting the presence of complementary sequences in a given sample. However, other uses are also envisioned, such as the use of the sequence information for the preparation of mutant species primers, or primers for use in preparing other genetic constructions.

Polynucleotide molecules having sequence regions consisting of contiguous nucleotide stretches of 10-14, 15-20, 30, 50, or even of 100-200 nucleotides or so (including intermediate lengths as well), identical or complementary to a polynucleotide sequence disclosed herein, are particularly contemplated as hybridization probes for use in, *e.g.*, Southern and Northern blotting. This would allow a gene product, or fragment thereof, to be analyzed, both in diverse cell types and also in various bacterial cells. The total size of fragment, as well as the size of the complementary stretch(es), will ultimately depend on the intended use or application of the particular nucleic acid segment. Smaller fragments will generally find use in hybridization embodiments, wherein the length of the contiguous complementary region

may be varied, such as between about 15 and about 100 nucleotides, but larger contiguous complementarity stretches may be used, according to the length complementary sequences one wishes to detect.

The use of a hybridization probe of about 15-25 nucleotides in length
5 allows the formation of a duplex molecule that is both stable and selective. Molecules having contiguous complementary sequences over stretches greater than 15 bases in length are generally preferred, though, in order to increase stability and selectivity of the hybrid, and thereby improve the quality and degree of specific hybrid molecules obtained. One will generally prefer to design nucleic acid molecules having gene-
10 complementary stretches of 15 to 25 contiguous nucleotides, or even longer where desired.

Hybridization probes may be selected from any portion of any of the sequences disclosed herein. All that is required is to review the sequences set forth herein, or to any continuous portion of the sequences, from about 15-25 nucleotides in
15 length up to and including the full length sequence, that one wishes to utilize as a probe or primer. The choice of probe and primer sequences may be governed by various factors. For example, one may wish to employ primers from towards the termini of the total sequence.

Small polynucleotide segments or fragments may be readily prepared by,
20 for example, directly synthesizing the fragment by chemical means, as is commonly practiced using an automated oligonucleotide synthesizer. Also, fragments may be obtained by application of nucleic acid reproduction technology, such as the PCRTM technology of U. S. Patent 4,683,202 (incorporated herein by reference), by introducing selected sequences into recombinant vectors for recombinant production, and by other
25 recombinant DNA techniques generally known to those of skill in the art of molecular biology.

The nucleotide sequences of the invention may be used for their ability to selectively form duplex molecules with complementary stretches of the entire gene or gene fragments of interest. Depending on the application envisioned, one will typically
30 desire to employ varying conditions of hybridization to achieve varying degrees of selectivity of probe towards target sequence. For applications requiring high selectivity,

one will typically desire to employ relatively stringent conditions to form the hybrids, e.g., one will select relatively low salt and/or high temperature conditions, such as provided by a salt concentration of from about 0.02 M to about 0.15 M salt at temperatures of from about 50°C to about 70°C. Such selective conditions tolerate
5 little, if any, mismatch between the probe and the template or target strand, and would be particularly suitable for isolating related sequences.

Of course, for some applications, for example, where one desires to prepare mutants employing a mutant primer strand hybridized to an underlying template, less stringent (reduced stringency) hybridization conditions will typically be
10 needed in order to allow formation of the heteroduplex. In these circumstances, one may desire to employ salt conditions such as those of from about 0.15 M to about 0.9 M salt, at temperatures ranging from about 20°C to about 55°C. Cross-hybridizing species can thereby be readily identified as positively hybridizing signals with respect to control hybridizations. In any case, it is generally appreciated that conditions can be rendered
15 more stringent by the addition of increasing amounts of formamide, which serves to destabilize the hybrid duplex in the same manner as increased temperature. Thus, hybridization conditions can be readily manipulated, and thus will generally be a method of choice depending on the desired results.

According to another embodiment of the present invention,
20 polynucleotide compositions comprising antisense oligonucleotides are provided. Antisense oligonucleotides have been demonstrated to be effective and targeted inhibitors of protein synthesis, and, consequently, provide a therapeutic approach by which a disease can be treated by inhibiting the synthesis of proteins that contribute to the disease. The efficacy of antisense oligonucleotides for inhibiting protein synthesis
25 is well established. For example, the synthesis of polygalacturonase and the muscarine type 2 acetylcholine receptor are inhibited by antisense oligonucleotides directed to their respective mRNA sequences (U. S. Patent 5,739,119 and U. S. Patent 5,759,829). Further, examples of antisense inhibition have been demonstrated with the nuclear protein cyclin, the multiple drug resistance gene (MDG1), ICAM-1, E-selectin, STK-1,
30 striatal GABA_A receptor and human EGF (Jaskulski *et al.*, Science. 1988 Jun 10;240(4858):1544-6; Vasanthakumar and Ahmed, Cancer Commun. 1989;1(4):225-

32; Peris *et al.*, Brain Res Mol Brain Res. 1998 Jun 15;57(2):310-20; U. S. Patent 5,801,154; U.S. Patent 5,789,573; U. S. Patent 5,718,709 and U.S. Patent 5,610,288). Antisense constructs have also been described that inhibit and can be used to treat a variety of abnormal cellular proliferations, *e.g.* cancer (U. S. Patent 5,747,470; U. S. Patent 5,591,317 and U. S. Patent 5,783,683).

Therefore, in certain embodiments, the present invention provides oligonucleotide sequences that comprise all, or a portion of, any sequence that is capable of specifically binding to polynucleotide sequence described herein, or a complement thereof. In one embodiment, the antisense oligonucleotides comprise DNA or derivatives thereof. In another embodiment, the oligonucleotides comprise RNA or derivatives thereof. In a third embodiment, the oligonucleotides are modified DNAs comprising a phosphorothioated modified backbone. In a fourth embodiment, the oligonucleotide sequences comprise peptide nucleic acids or derivatives thereof. In each case, preferred compositions comprise a sequence region that is complementary, and more preferably substantially-complementary, and even more preferably, completely complementary to one or more portions of polynucleotides disclosed herein. Selection of antisense compositions specific for a given gene sequence is based upon analysis of the chosen target sequence and determination of secondary structure, T_m , binding energy, and relative stability. Antisense compositions may be selected based upon their relative inability to form dimers, hairpins, or other secondary structures that would reduce or prohibit specific binding to the target mRNA in a host cell. Highly preferred target regions of the mRNA, are those which are at or near the AUG translation initiation codon, and those sequences which are substantially complementary to 5' regions of the mRNA. These secondary structure analyses and target site selection considerations can be performed, for example, using v.4 of the OLIGO primer analysis software and/or the BLASTN 2.0.5 algorithm software (Altschul *et al.*, Nucleic Acids Res. 1997, 25(17):3389-402).

The use of an antisense delivery method employing a short peptide vector, termed MPG (27 residues), is also contemplated. The MPG peptide contains a hydrophobic domain derived from the fusion sequence of HIV gp41 and a hydrophilic domain from the nuclear localization sequence of SV40 T-antigen (Morris *et al.*,

Nucleic Acids Res. 1997 Jul 15;25(14):2730-6). It has been demonstrated that several molecules of the MPG peptide coat the antisense oligonucleotides and can be delivered into cultured mammalian cells in less than 1 hour with relatively high efficiency (90%). Further, the interaction with MPG strongly increases both the stability of the oligonucleotide to nuclease and the ability to cross the plasma membrane.

According to another embodiment of the invention, the polynucleotide compositions described herein are used in the design and preparation of ribozyme molecules for inhibiting expression of the tumor polypeptides and proteins of the present invention in tumor cells. Ribozymes are RNA-protein complexes that cleave nucleic acids in a site-specific fashion. Ribozymes have specific catalytic domains that possess endonuclease activity (Kim and Cech, Proc Natl Acad Sci U S A. 1987 Dec;84(24):8788-92; Forster and Symons, Cell. 1987 Apr 24;49(2):211-20). For example, a large number of ribozymes accelerate phosphoester transfer reactions with a high degree of specificity, often cleaving only one of several phosphoesters in an oligonucleotide substrate (Cech *et al.*, Cell. 1981 Dec;27(3 Pt 2):487-96; Michel and Westhof, J Mol Biol. 1990 Dec 5;216(3):585-610; Reinhold-Hurek and Shub, Nature. 1992 May 14;357(6374):173-6). This specificity has been attributed to the requirement that the substrate bind via specific base-pairing interactions to the internal guide sequence ("IGS") of the ribozyme prior to chemical reaction.

Six basic varieties of naturally-occurring enzymatic RNAs are known presently. Each can catalyze the hydrolysis of RNA phosphodiester bonds *in trans* (and thus can cleave other RNA molecules) under physiological conditions. In general, enzymatic nucleic acids act by first binding to a target RNA. Such binding occurs through the target binding portion of a enzymatic nucleic acid which is held in close proximity to an enzymatic portion of the molecule that acts to cleave the target RNA. Thus, the enzymatic nucleic acid first recognizes and then binds a target RNA through complementary base-pairing, and once bound to the correct site, acts enzymatically to cut the target RNA. Strategic cleavage of such a target RNA will destroy its ability to direct synthesis of an encoded protein. After an enzymatic nucleic acid has bound and cleaved its RNA target, it is released from that RNA to search for another target and can repeatedly bind and cleave new targets.

The enzymatic nature of a ribozyme is advantageous over many technologies, such as antisense technology (where a nucleic acid molecule simply binds to a nucleic acid target to block its translation) since the concentration of ribozyme necessary to affect a therapeutic treatment is lower than that of an antisense oligonucleotide. This advantage reflects the ability of the ribozyme to act enzymatically. Thus, a single ribozyme molecule is able to cleave many molecules of target RNA. In addition, the ribozyme is a highly specific inhibitor, with the specificity of inhibition depending not only on the base pairing mechanism of binding to the target RNA, but also on the mechanism of target RNA cleavage. Single mismatches, or base-substitutions, near the site of cleavage can completely eliminate catalytic activity of a ribozyme. Similar mismatches in antisense molecules do not prevent their action (Woolf *et al.*, Proc Natl Acad Sci U S A. 1992 Aug 15;89(16):7305-9). Thus, the specificity of action of a ribozyme is greater than that of an antisense oligonucleotide binding the same RNA site.

The enzymatic nucleic acid molecule may be formed in a hammerhead, hairpin, a hepatitis δ virus, group I intron or RNaseP RNA (in association with an RNA guide sequence) or Neurospora VS RNA motif. Examples of hammerhead motifs are described by Rossi *et al.* Nucleic Acids Res. 1992 Sep 11;20(17):4559-65. Examples of hairpin motifs are described by Hampel *et al.* (Eur. Pat. Appl. Publ. No. EP 0360257), Hampel and Tritz, Biochemistry 1989 Jun 13;28(12):4929-33; Hampel *et al.*, Nucleic Acids Res. 1990 Jan 25;18(2):299-304 and U. S. Patent 5,631,359. An example of the hepatitis δ virus motif is described by Perrotta and Been, Biochemistry. 1992 Dec 1;31(47):11843-52; an example of the RNaseP motif is described by Guerrier-Takada *et al.*, Cell. 1983 Dec;35(3 Pt 2):849-57; Neurospora VS RNA ribozyme motif is described by Collins (Saville and Collins, Cell. 1990 May 18;61(4):685-96; Saville and Collins, Proc Natl Acad Sci U S A. 1991 Oct 1;88(19):8826-30; Collins and Olive, Biochemistry. 1993 Mar 23;32(11):2795-9); and an example of the Group I intron is described in (U. S. Patent 4,987,071). All that is important in an enzymatic nucleic acid molecule of this invention is that it has a specific substrate binding site which is complementary to one or more of the target gene RNA regions, and that it have nucleotide sequences within or surrounding that substrate binding site which impart an

RNA cleaving activity to the molecule. Thus the ribozyme constructs need not be limited to specific motifs mentioned herein.

Ribozymes may be designed as described in Int. Pat. Appl. Publ. No. WO 93/23569 and Int. Pat. Appl. Publ. No. WO 94/02595, each specifically incorporated herein by reference) and synthesized to be tested *in vitro* and *in vivo*, as described. Such ribozymes can also be optimized for delivery. While specific examples are provided, those in the art will recognize that equivalent RNA targets in other species can be utilized when necessary.

Ribozyme activity can be optimized by altering the length of the ribozyme binding arms, or chemically synthesizing ribozymes with modifications that prevent their degradation by serum ribonucleases (see *e.g.*, Int. Pat. Appl. Publ. No. WO 92/07065; Int. Pat. Appl. Publ. No. WO 93/15187; Int. Pat. Appl. Publ. No. WO 91/03162; Eur. Pat. Appl. Publ. No. 92110298.4; U. S. Patent 5,334,711; and Int. Pat. Appl. Publ. No. WO 94/13688, which describe various chemical modifications that can be made to the sugar moieties of enzymatic RNA molecules), modifications which enhance their efficacy in cells, and removal of stem II bases to shorten RNA synthesis times and reduce chemical requirements.

Sullivan *et al.* (Int. Pat. Appl. Publ. No. WO 94/02595) describes the general methods for delivery of enzymatic RNA molecules. Ribozymes may be administered to cells by a variety of methods known to those familiar to the art, including, but not restricted to, encapsulation in liposomes, by iontophoresis, or by incorporation into other vehicles, such as hydrogels, cyclodextrins, biodegradable nanocapsules, and bioadhesive microspheres. For some indications, ribozymes may be directly delivered *ex vivo* to cells or tissues with or without the aforementioned vehicles. Alternatively, the RNA/vehicle combination may be locally delivered by direct inhalation, by direct injection or by use of a catheter, infusion pump or stint. Other routes of delivery include, but are not limited to, intravascular, intramuscular, subcutaneous or joint injection, aerosol inhalation, oral (tablet or pill form), topical, systemic, ocular, intraperitoneal and/or intrathecal delivery. More detailed descriptions of ribozyme delivery and administration are provided in Int. Pat. Appl. Publ. No. WO

94/02595 and Int. Pat. Appl. Publ. No. WO 93/23569, each specifically incorporated herein by reference.

Another means of accumulating high concentrations of a ribozyme(s) within cells is to incorporate the ribozyme-encoding sequences into a DNA expression
5 vector. Transcription of the ribozyme sequences are driven from a promoter for eukaryotic RNA polymerase I (pol I), RNA polymerase II (pol II), or RNA polymerase III (pol III). Transcripts from pol II or pol III promoters will be expressed at high levels in all cells; the levels of a given pol II promoter in a given cell type will depend on the nature of the gene regulatory sequences (enhancers, silencers, *etc.*) present nearby.
10 Prokaryotic RNA polymerase promoters may also be used, providing that the prokaryotic RNA polymerase enzyme is expressed in the appropriate cells. Ribozymes expressed from such promoters have been shown to function in mammalian cells. Such transcription units can be incorporated into a variety of vectors for introduction into mammalian cells, including but not restricted to, plasmid DNA vectors, viral DNA
15 vectors (such as adenovirus or adeno-associated vectors), or viral RNA vectors (such as retroviral, semliki forest virus, sindbis virus vectors).

In another embodiment of the invention, peptide nucleic acids (PNAs) compositions are provided. PNA is a DNA mimic in which the nucleobases are attached to a pseudopeptide backbone (Good and Nielsen, *Antisense Nucleic Acid Drug*
20 *Dev.* 1997 7(4) 431-37). PNA is able to be utilized in a number methods that traditionally have used RNA or DNA. Often PNA sequences perform better in techniques than the corresponding RNA or DNA sequences and have utilities that are not inherent to RNA or DNA. A review of PNA including methods of making, characteristics of, and methods of using, is provided by Corey (*Trends Biotechnol* 1997
25 Jun;15(6):224-9). As such, in certain embodiments, one may prepare PNA sequences that are complementary to one or more portions of the ACE mRNA sequence, and such PNA compositions may be used to regulate, alter, decrease, or reduce the translation of ACE-specific mRNA, and thereby alter the level of ACE activity in a host cell to which such PNA compositions have been administered.

30 PNAs have 2-aminoethyl-glycine linkages replacing the normal phosphodiester backbone of DNA (Nielsen *et al.*, *Science* 1991 Dec 6;254(5037):1497-

500; Hanvey *et al.*, Science. 1992 Nov 27;258(5087):1481-5; Hyrup and Nielsen, Bioorg Med Chem. 1996 Jan;4(1):5-23). This chemistry has three important consequences: firstly, in contrast to DNA or phosphorothioate oligonucleotides, PNAs are neutral molecules; secondly, PNAs are achiral, which avoids the need to develop a stereoselective synthesis; and thirdly, PNA synthesis uses standard Boc or Fmoc protocols for solid-phase peptide synthesis, although other methods, including a modified Merrifield method, have been used.

PNA monomers or ready-made oligomers are commercially available from PerSeptive Biosystems (Framingham, MA). PNA syntheses by either Boc or Fmoc protocols are straightforward using manual or automated protocols (Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45). The manual protocol lends itself to the production of chemically modified PNAs or the simultaneous synthesis of families of closely related PNAs.

As with peptide synthesis, the success of a particular PNA synthesis will depend on the properties of the chosen sequence. For example, while in theory PNAs can incorporate any combination of nucleotide bases, the presence of adjacent purines can lead to deletions of one or more residues in the product. In expectation of this difficulty, it is suggested that, in producing PNAs with adjacent purines, one should repeat the coupling of residues likely to be added inefficiently. This should be followed by the purification of PNAs by reverse-phase high-pressure liquid chromatography, providing yields and purity of product similar to those observed during the synthesis of peptides.

Modifications of PNAs for a given application may be accomplished by coupling amino acids during solid-phase synthesis or by attaching compounds that contain a carboxylic acid group to the exposed N-terminal amine. Alternatively, PNAs can be modified after synthesis by coupling to an introduced lysine or cysteine. The ease with which PNAs can be modified facilitates optimization for better solubility or for specific functional requirements. Once synthesized, the identity of PNAs and their derivatives can be confirmed by mass spectrometry. Several studies have made and utilized modifications of PNAs (for example, Norton *et al.*, Bioorg Med Chem. 1995 Apr;3(4):437-45; Petersen *et al.*, J Pept Sci. 1995 May-Jun;1(3):175-83; Orum *et al.*,

- Biotechniques. 1995 Sep;19(3):472-80; Footer *et al.*, Biochemistry. 1996 Aug 20;35(33):10673-9; Griffith *et al.*, Nucleic Acids Res. 1995 Aug 11;23(15):3003-8; Pardridge *et al.*, Proc Natl Acad Sci U S A. 1995 Jun 6;92(12):5592-6; Boffa *et al.*, Proc Natl Acad Sci U S A. 1995 Mar 14;92(6):1901-5; Gambacorti-Passerini *et al.*, Blood. 1996 Aug 15;88(4):1411-7; Armitage *et al.*, Proc Natl Acad Sci U S A. 1997 Nov 11;94(23):12320-5; Seeger *et al.*, Biotechniques. 1997 Sep;23(3):512-7). U.S. Patent No. 5,700,922 discusses PNA-DNA-PNA chimeric molecules and their uses in diagnostics, modulating protein in organisms, and treatment of conditions susceptible to therapeutics.
- 10 Methods of characterizing the antisense binding properties of PNAs are discussed in Rose (Anal Chem. 1993 Dec 15;65(24):3545-9) and Jensen *et al.* (Biochemistry. 1997 Apr 22;36(16):5072-7). Rose uses capillary gel electrophoresis to determine binding of PNAs to their complementary oligonucleotide, measuring the relative binding kinetics and stoichiometry. Similar types of measurements were made
- 15 by Jensen *et al.* using BIAcore™ technology.

Other applications of PNAs that have been described and will be apparent to the skilled artisan include use in DNA strand invasion, antisense inhibition, mutational analysis, enhancers of transcription, nucleic acid purification, isolation of transcriptionally active genes, blocking of transcription factor binding, genome

20 cleavage, biosensors, *in situ* hybridization, and the like.

Polynucleotide Identification, Characterization and Expression

Polynucleotides compositions of the present invention may be identified, prepared and/or manipulated using any of a variety of well established techniques (see generally, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989, and other like references). For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least two fold greater in a tumor than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed, for example,

30 using the microarray technology of Affymetrix, Inc. (Santa Clara, CA) according to the

manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Alternatively, polynucleotides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as tumor cells.

5 Many template dependent processes are available to amplify a target sequences of interest present in a sample. One of the best known amplification methods is the polymerase chain reaction (PCR™) which is described in detail in U.S. Patent Nos. 4,683,195, 4,683,202 and 4,800,159, each of which is incorporated herein by reference in its entirety. Briefly, in PCR™, two primer sequences are prepared which
10 are complementary to regions on opposite complementary strands of the target sequence. An excess of deoxynucleoside triphosphates is added to a reaction mixture along with a DNA polymerase (*e.g.*, *Taq* polymerase). If the target sequence is present in a sample, the primers will bind to the target and the polymerase will cause the primers to be extended along the target sequence by adding on nucleotides. By raising
15 and lowering the temperature of the reaction mixture, the extended primers will dissociate from the target to form reaction products, excess primers will bind to the target and to the reaction product and the process is repeated. Preferably reverse transcription and PCR™ amplification procedure may be performed in order to quantify the amount of mRNA amplified. Polymerase chain reaction methodologies are well
20 known in the art.

Any of a number of other template dependent processes, many of which are variations of the PCR™ amplification technique, are readily known and available in the art. Illustratively, some such methods include the ligase chain reaction (referred to as LCR), described, for example, in Eur. Pat. Appl. Publ. No. 320,308 and U.S. Patent
25 No. 4,883,750; Qbeta Replicase, described in PCT Intl. Pat. Appl. Publ. No. PCT/US87/00880; Strand Displacement Amplification (SDA) and Repair Chain Reaction (RCR). Still other amplification methods are described in Great Britain Pat. Appl. No. 2 202 328, and in PCT Intl. Pat. Appl. Publ. No. PCT/US89/01025. Other nucleic acid amplification procedures include transcription-based amplification systems
30 (TAS) (PCT Intl. Pat. Appl. Publ. No. WO 88/10315), including nucleic acid sequence based amplification (NASBA) and 3SR. Eur. Pat. Appl. Publ. No. 329,822 describes a

nucleic acid amplification process involving cyclically synthesizing single-stranded RNA ("ssRNA"), ssDNA, and double-stranded DNA (dsDNA). PCT Intl. Pat. Appl. Publ. No. WO 89/06700 describes a nucleic acid sequence amplification scheme based on the hybridization of a promoter/primer sequence to a target single-stranded DNA ("ssDNA") followed by transcription of many RNA copies of the sequence. Other
5 amplification methods such as "RACE" (Frohman, 1990), and "one-sided PCR" (Ohara, 1989) are also well-known to those of skill in the art.

An amplified portion of a polynucleotide of the present invention may be used to isolate a full length gene from a suitable library (e.g., a tumor cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is
10 screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (e.g., by
15 nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then generally screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (see Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor
20 Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The
25 complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences can then be assembled into a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, amplification techniques, such as those described above,
30 can be useful for obtaining a full length coding sequence from a partial cDNA sequence. One such amplification technique is inverse PCR (see Triglia et al., *Nucl. Acids Res.*

16:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be
5 retrieved by amplification with a primer to a linker sequence and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO
10 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids.*
15 *Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be
20 performed using well known programs (e.g., NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

In other embodiments of the invention, polynucleotide sequences or fragments thereof which encode polypeptides of the invention, or fusion proteins or
25 functional equivalents thereof, may be used in recombinant DNA molecules to direct expression of a polypeptide in appropriate host cells. Due to the inherent degeneracy of the genetic code, other DNA sequences that encode substantially the same or a functionally equivalent amino acid sequence may be produced and these sequences may be used to clone and express a given polypeptide.

30 As will be understood by those of skill in the art, it may be advantageous in some instances to produce polypeptide-encoding nucleotide sequences possessing

non-naturally occurring codons. For example, codons preferred by a particular prokaryotic or eukaryotic host can be selected to increase the rate of protein expression or to produce a recombinant RNA transcript having desirable properties, such as a half-life which is longer than that of a transcript generated from the naturally occurring
5 sequence.

Moreover, the polynucleotide sequences of the present invention can be engineered using methods generally known in the art in order to alter polypeptide encoding sequences for a variety of reasons, including but not limited to, alterations which modify the cloning, processing, and/or expression of the gene product. For
10 example, DNA shuffling by random fragmentation and PCR reassembly of gene fragments and synthetic oligonucleotides may be used to engineer the nucleotide sequences. In addition, site-directed mutagenesis may be used to insert new restriction sites, alter glycosylation patterns, change codon preference, produce splice variants, or introduce mutations, and so forth.

In another embodiment of the invention, natural, modified, or recombinant nucleic acid sequences may be ligated to a heterologous sequence to encode a fusion protein. For example, to screen peptide libraries for inhibitors of polypeptide activity, it may be useful to encode a chimeric protein that can be recognized by a commercially available antibody. A fusion protein may also be
15 engineered to contain a cleavage site located between the polypeptide-encoding sequence and the heterologous protein sequence, so that the polypeptide may be cleaved and purified away from the heterologous moiety.

Sequences encoding a desired polypeptide may be synthesized, in whole or in part, using chemical methods well known in the art (see Caruthers, M. H. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 215-223, Horn, T. et al. (1980) *Nucl. Acids Res. Symp. Ser.* 225-232). Alternatively, the protein itself may be produced using chemical methods to synthesize the amino acid sequence of a polypeptide, or a portion thereof. For example, peptide synthesis can be performed using various solid-phase techniques (Roberge, J. Y. et al. (1995) *Science* 269:202-204) and automated synthesis may be
20 achieved, for example, using the ABI 431A Peptide Synthesizer (Perkin Elmer, Palo Alto, CA).

A newly synthesized peptide may be substantially purified by preparative high performance liquid chromatography (e.g., Creighton, T. (1983) *Proteins, Structures and Molecular Principles*, WH Freeman and Co., New York, N.Y.) or other comparable techniques available in the art. The composition of the synthetic peptides may be confirmed by amino acid analysis or sequencing (e.g., the Edman degradation procedure). Additionally, the amino acid sequence of a polypeptide, or any part thereof, may be altered during direct synthesis and/or combined using chemical methods with sequences from other proteins, or any part thereof, to produce a variant polypeptide.

In order to express a desired polypeptide, the nucleotide sequences encoding the polypeptide, or functional equivalents, may be inserted into appropriate expression vector, i.e., a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. Methods which are well known to those skilled in the art may be used to construct expression vectors containing sequences encoding a polypeptide of interest and appropriate transcriptional and translational control elements. These methods include *in vitro* recombinant DNA techniques, synthetic techniques, and *in vivo* genetic recombination. Such techniques are described, for example, in Sambrook, J. et al. (1989) *Molecular Cloning, A Laboratory Manual*, Cold Spring Harbor Press, Plainview, N.Y., and Ausubel, F. M. et al. (1989) *Current Protocols in Molecular Biology*, John Wiley & Sons, New York, N.Y.

A variety of expression vector/host systems may be utilized to contain and express polynucleotide sequences. These include, but are not limited to, microorganisms such as bacteria transformed with recombinant bacteriophage, plasmid, or cosmid DNA expression vectors; yeast transformed with yeast expression vectors; insect cell systems infected with virus expression vectors (e.g., baculovirus); plant cell systems transformed with virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or with bacterial expression vectors (e.g., Ti or pBR322 plasmids); or animal cell systems.

The "control elements" or "regulatory sequences" present in an expression vector are those non-translated regions of the vector--enhancers, promoters, 5' and 3' untranslated regions--which interact with host cellular proteins to carry out

transcription and translation. Such elements may vary in their strength and specificity. Depending on the vector system and host utilized, any number of suitable transcription and translation elements, including constitutive and inducible promoters, may be used. For example, when cloning in bacterial systems, inducible promoters such as the hybrid
5 lacZ promoter of the PBLUESCRIPT phagemid (Stratagene, La Jolla, Calif.) or
PSPORT1 plasmid (Gibco BRL, Gaithersburg, MD) and the like may be used. In
mammalian cell systems, promoters from mammalian genes or from mammalian viruses
are generally preferred. If it is necessary to generate a cell line that contains multiple
copies of the sequence encoding a polypeptide, vectors based on SV40 or EBV may be
10 advantageously used with an appropriate selectable marker.

In bacterial systems, any of a number of expression vectors may be
selected depending upon the use intended for the expressed polypeptide. For example,
when large quantities are needed, for example for the induction of antibodies, vectors
which direct high level expression of fusion proteins that are readily purified may be
15 used. Such vectors include, but are not limited to, the multifunctional *E. coli* cloning
and expression vectors such as BLUESCRIPT (Stratagene), in which the sequence
encoding the polypeptide of interest may be ligated into the vector in frame with
sequences for the amino-terminal Met and the subsequent 7 residues of β -galactosidase
so that a hybrid protein is produced; pIN vectors (Van Heeke, G. and S.
20 M. Schuster (1989) *J. Biol. Chem.* 264:5503-5509); and the like. pGEX Vectors
(Promega, Madison, Wis.) may also be used to express foreign polypeptides as fusion
proteins with glutathione S-transferase (GST). In general, such fusion proteins are
soluble and can easily be purified from lysed cells by adsorption to glutathione-agarose
beads followed by elution in the presence of free glutathione. Proteins made in such
25 systems may be designed to include heparin, thrombin, or factor XA protease cleavage
sites so that the cloned polypeptide of interest can be released from the GST moiety at
will.

In the yeast, *Saccharomyces cerevisiae*, a number of vectors containing
constitutive or inducible promoters such as alpha factor, alcohol oxidase, and PGH may
30 be used. For reviews, see Ausubel et al. (supra) and Grant et al. (1987) *Methods*
Enzymol. 153:516-544.

In cases where plant expression vectors are used, the expression of sequences encoding polypeptides may be driven by any of a number of promoters. For example, viral promoters such as the 35S and 19S promoters of CaMV may be used alone or in combination with the omega leader sequence from TMV (Takamatsu, N. 5 (1987) *EMBO J.* 6:307-311. Alternatively, plant promoters such as the small subunit of RUBISCO or heat shock promoters may be used (Coruzzi, G. et al. (1984) *EMBO J.* 3:1671-1680; Broglie, R. et al. (1984) *Science* 224:838-843; and Winter, J. et al. (1991) *Results Probl. Cell Differ.* 17:85-105). These constructs can be introduced into plant cells by direct DNA transformation or pathogen-mediated transfection. Such techniques 10 are described in a number of generally available reviews (see, for example, Hobbs, S. or Murry, L. E. in McGraw Hill Yearbook of Science and Technology (1992) McGraw Hill, New York, N.Y.; pp. 191-196).

An insect system may also be used to express a polypeptide of interest. For example, in one such system, Autographa californica nuclear polyhedrosis virus 15 (AcNPV) is used as a vector to express foreign genes in Spodoptera frugiperda cells or in Trichoplusia larvae. The sequences encoding the polypeptide may be cloned into a non-essential region of the virus, such as the polyhedrin gene, and placed under control of the polyhedrin promoter. Successful insertion of the polypeptide-encoding sequence will render the polyhedrin gene inactive and produce recombinant virus lacking coat 20 protein. The recombinant viruses may then be used to infect, for example, S. frugiperda cells or Trichoplusia larvae in which the polypeptide of interest may be expressed (Engelhard, E. K. et al. (1994) *Proc. Natl. Acad. Sci.* 91 :3224-3227).

In mammalian host cells, a number of viral-based expression systems are generally available. For example, in cases where an adenovirus is used as an expression 25 vector, sequences encoding a polypeptide of interest may be ligated into an adenovirus transcription/translation complex consisting of the late promoter and tripartite leader sequence. Insertion in a non-essential E1 or E3 region of the viral genome may be used to obtain a viable virus which is capable of expressing the polypeptide in infected host cells (Logan, J. and Shenk, T. (1984) *Proc. Natl. Acad. Sci.* 81:3655-3659). In addition, 30 transcription enhancers, such as the Rous sarcoma virus (RSV) enhancer, may be used to increase expression in mammalian host cells.

Specific initiation signals may also be used to achieve more efficient translation of sequences encoding a polypeptide of interest. Such signals include the ATG initiation codon and adjacent sequences. In cases where sequences encoding the polypeptide, its initiation codon, and upstream sequences are inserted into the appropriate expression vector, no additional transcriptional or translational control signals may be needed. However, in cases where only coding sequence, or a portion thereof, is inserted, exogenous translational control signals including the ATG initiation codon should be provided. Furthermore, the initiation codon should be in the correct reading frame to ensure translation of the entire insert. Exogenous translational elements and initiation codons may be of various origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of enhancers which are appropriate for the particular cell system which is used, such as those described in the literature (Scharf, D. et al. (1994) *Results Probl. Cell Differ.* 20:125-162).

In addition, a host cell strain may be chosen for its ability to modulate the expression of the inserted sequences or to process the expressed protein in the desired fashion. Such modifications of the polypeptide include, but are not limited to, acetylation, carboxylation, glycosylation, phosphorylation, lipidation, and acylation. Post-translational processing which cleaves a "prepro" form of the protein may also be used to facilitate correct insertion, folding and/or function. Different host cells such as CHO, COS, HeLa, MDCK, HEK293, and WI38, which have specific cellular machinery and characteristic mechanisms for such post-translational activities, may be chosen to ensure the correct modification and processing of the foreign protein.

For long-term, high-yield production of recombinant proteins, stable expression is generally preferred. For example, cell lines which stably express a polynucleotide of interest may be transformed using expression vectors which may contain viral origins of replication and/or endogenous expression elements and a selectable marker gene on the same or on a separate vector. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth and recovery of cells which

successfully express the introduced sequences. Resistant clones of stably transformed cells may be proliferated using tissue culture techniques appropriate to the cell type.

Any number of selection systems may be used to recover transformed cell lines. These include, but are not limited to, the herpes simplex virus thymidine kinase (Wigler, M. et al. (1977) *Cell* 11:223-32) and adenine phosphoribosyltransferase (Lowy, I. et al. (1990) *Cell* 22:817-23) genes which can be employed in tk.sup.- or aprt.sup.- cells, respectively. Also, antimetabolite, antibiotic or herbicide resistance can be used as the basis for selection; for example, dhfr which confers resistance to methotrexate (Wigler, M. et al. (1980) *Proc. Natl. Acad. Sci.* 77:3567-70); npt, which confers resistance to the aminoglycosides, neomycin and G-418 (Colbere-Garapin, F. et al (1981) *J. Mol. Biol.* 150:1-14); and als or pat, which confer resistance to chlorsulfuron and phosphinotricin acetyltransferase, respectively (Murry, *supra*). Additional selectable genes have been described, for example, trpB, which allows cells to utilize indole in place of tryptophan, or hisD, which allows cells to utilize histinol in place of histidine (Hartman, S. C. and R. C. Mulligan (1988) *Proc. Natl. Acad. Sci.* 85:8047-51). The use of visible markers has gained popularity with such markers as anthocyanins, beta-glucuronidase and its substrate GUS, and luciferase and its substrate luciferin, being widely used not only to identify transformants, but also to quantify the amount of transient or stable protein expression attributable to a specific vector system (Rhodes, C. A. et al. (1995) *Methods Mol. Biol.* 55:121-131).

Although the presence/absence of marker gene expression suggests that the gene of interest is also present, its presence and expression may need to be confirmed. For example, if the sequence encoding a polypeptide is inserted within a marker gene sequence, recombinant cells containing sequences can be identified by the absence of marker gene function. Alternatively, a marker gene can be placed in tandem with a polypeptide-encoding sequence under the control of a single promoter. Expression of the marker gene in response to induction or selection usually indicates expression of the tandem gene as well.

Alternatively, host cells that contain and express a desired polynucleotide sequence may be identified by a variety of procedures known to those of skill in the art. These procedures include, but are not limited to, DNA-DNA or DNA-

RNA hybridizations and protein bioassay or immunoassay techniques which include, for example, membrane, solution, or chip based technologies for the detection and/or quantification of nucleic acid or protein.

A variety of protocols for detecting and measuring the expression of
5 polynucleotide-encoded products, using either polyclonal or monoclonal antibodies specific for the product are known in the art. Examples include enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA), and fluorescence activated cell sorting (FACS). A two-site, monoclonal-based immunoassay utilizing monoclonal antibodies reactive to two non-interfering epitopes on a given polypeptide may be
10 preferred for some applications, but a competitive binding assay may also be employed. These and other assays are described, among other places, in Hampton, R. et al. (1990; Serological Methods, a Laboratory Manual, APS Press, St Paul. Minn.) and Maddox, D. E. et al. (1983; *J. Exp. Med.* 158:1211-1216).

A wide variety of labels and conjugation techniques are known by those
15 skilled in the art and may be used in various nucleic acid and amino acid assays. Means for producing labeled hybridization or PCR probes for detecting sequences related to polynucleotides include oligolabeling, nick translation, end-labeling or PCR amplification using a labeled nucleotide. Alternatively, the sequences, or any portions thereof may be cloned into a vector for the production of an mRNA probe. Such vectors
20 are known in the art, are commercially available, and may be used to synthesize RNA probes in vitro by addition of an appropriate RNA polymerase such as T7, T3, or SP6 and labeled nucleotides. These procedures may be conducted using a variety of commercially available kits. Suitable reporter molecules or labels, which may be used include radionuclides, enzymes, fluorescent, chemiluminescent, or chromogenic agents
25 as well as substrates, cofactors, inhibitors, magnetic particles, and the like.

Host cells transformed with a polynucleotide sequence of interest may be cultured under conditions suitable for the expression and recovery of the protein from cell culture. The protein produced by a recombinant cell may be secreted or contained intracellularly depending on the sequence and/or the vector used. As will be understood
30 by those of skill in the art, expression vectors containing polynucleotides of the invention may be designed to contain signal sequences which direct secretion of the

encoded polypeptide through a prokaryotic or eukaryotic cell membrane. Other recombinant constructions may be used to join sequences encoding a polypeptide of interest to nucleotide sequence encoding a polypeptide domain which will facilitate purification of soluble proteins. Such purification facilitating domains include, but are not limited to, metal chelating peptides such as histidine-tryptophan modules that allow purification on immobilized metals, protein A domains that allow purification on immobilized immunoglobulin, and the domain utilized in the FLAGS extension/affinity purification system (Immunex Corp., Seattle, Wash.). The inclusion of cleavable linker sequences such as those specific for Factor XA or enterokinase (Invitrogen, San Diego, Calif.) between the purification domain and the encoded polypeptide may be used to facilitate purification. One such expression vector provides for expression of a fusion protein containing a polypeptide of interest and a nucleic acid encoding 6 histidine residues preceding a thioredoxin or an enterokinase cleavage site. The histidine residues facilitate purification on IMIAC (immobilized metal ion affinity chromatography) as described in Porath, J. et al. (1992, *Prot. Exp. Purif.* 3:263-281) while the enterokinase cleavage site provides a means for purifying the desired polypeptide from the fusion protein. A discussion of vectors which contain fusion proteins is provided in Kroll, D. J. et al. (1993; *DNA Cell Biol.* 12:441-453).

In addition to recombinant production methods, polypeptides of the invention, and fragments thereof, may be produced by direct peptide synthesis using solid-phase techniques (Merrifield J. (1963) *J. Am. Chem. Soc.* 85:2149-2154). Protein synthesis may be performed using manual techniques or by automation. Automated synthesis may be achieved, for example, using Applied Biosystems 431A Peptide Synthesizer (Perkin Elmer). Alternatively, various fragments may be chemically synthesized separately and combined using chemical methods to produce the full length molecule.

Antibody Compositions, Fragments Thereof and Other Binding Agents

According to another aspect, the present invention further provides binding agents, such as antibodies and antigen-binding fragments thereof, that exhibit immunological binding to a tumor polypeptide disclosed herein, or to a portion, variant

or derivative thereof. An antibody, or antigen-binding fragment thereof, is said to "specifically bind," "immunologically bind," and/or is "immunologically reactive" to a polypeptide of the invention if it reacts at a detectable level (within, for example, an ELISA assay) with the polypeptide, and does not react detectably with unrelated polypeptides under similar conditions.

Immunological binding, as used in this context, generally refers to the non-covalent interactions of the type which occur between an immunoglobulin molecule and an antigen for which the immunoglobulin is specific. The strength, or affinity of immunological binding interactions can be expressed in terms of the dissociation constant (K_d) of the interaction, wherein a smaller K_d represents a greater affinity. Immunological binding properties of selected polypeptides can be quantified using methods well known in the art. One such method entails measuring the rates of antigen-binding site/antigen complex formation and dissociation, wherein those rates depend on the concentrations of the complex partners, the affinity of the interaction, and on geometric parameters that equally influence the rate in both directions. Thus, both the "on rate constant" (K_{on}) and the "off rate constant" (K_{off}) can be determined by calculation of the concentrations and the actual rates of association and dissociation. The ratio of K_{off}/K_{on} enables cancellation of all parameters not related to affinity, and is thus equal to the dissociation constant K_d . See, generally, Davies et al. (1990) Annual Rev. Biochem. 59:439-473.

An "antigen-binding site," or "binding portion" of an antibody refers to the part of the immunoglobulin molecule that participates in antigen binding. The antigen binding site is formed by amino acid residues of the N-terminal variable ("V") regions of the heavy ("H") and light ("L") chains. Three highly divergent stretches within the V regions of the heavy and light chains are referred to as "hypervariable regions" which are interposed between more conserved flanking stretches known as "framework regions," or "FRs". Thus the term "FR" refers to amino acid sequences which are naturally found between and adjacent to hypervariable regions in immunoglobulins. In an antibody molecule, the three hypervariable regions of a light chain and the three hypervariable regions of a heavy chain are disposed relative to each other in three dimensional space to form an antigen-binding surface. The antigen-

binding surface is complementary to the three-dimensional surface of a bound antigen, and the three hypervariable regions of each of the heavy and light chains are referred to as "complementarity-determining regions," or "CDRs."

Binding agents may be further capable of differentiating between patients
5 with and without a cancer, such as lung cancer, using the representative assays provided herein. For example, antibodies or other binding agents that bind to a tumor protein will preferably generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, more preferably at least about 30% of patients. Alternatively, or in addition, the antibody will generate a negative signal indicating
10 absence of the disease in at least about 90% of individuals without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (*e.g.*, blood, sera, sputum, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. Preferably, a statistically
15 significant number of samples with and without the disease will be assayed. Each binding agent should satisfy the above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent.
20 For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.*, Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In
25 general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.*, mice, rats, rabbits, sheep
30 or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a

superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically.

- 5 Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

- Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.
- 15
20

- Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.
- 25
30

A number of therapeutically useful molecules are known in the art which comprise antigen-binding sites that are capable of exhibiting immunological binding properties of an antibody molecule. The proteolytic enzyme papain preferentially cleaves IgG molecules to yield several fragments, two of which (the "F(ab)" fragments) each comprise a covalent heterodimer that includes an intact antigen-binding site. The enzyme pepsin is able to cleave IgG molecules to provide several fragments, including the "F(ab')₂" fragment which comprises both antigen-binding sites. An "Fv" fragment can be produced by preferential proteolytic cleavage of an IgM, and on rare occasions IgG or IgA immunoglobulin molecule. Fv fragments are, however, more commonly derived using recombinant techniques known in the art. The Fv fragment includes a non-covalent V_H::V_L heterodimer including an antigen-binding site which retains much of the antigen recognition and binding capabilities of the native antibody molecule. Inbar et al. (1972) Proc. Nat. Acad. Sci. USA 69:2659-2662; Hochman et al. (1976) Biochem 15:2706-2710; and Ehrlich et al. (1980) Biochem 19:4091-4096.

A single chain Fv ("sFv") polypeptide is a covalently linked V_H::V_L heterodimer which is expressed from a gene fusion including V_H- and V_L-encoding genes linked by a peptide-encoding linker. Huston et al. (1988) Proc. Nat. Acad. Sci. USA 85(16):5879-5883. A number of methods have been described to discern chemical structures for converting the naturally aggregated--but chemically separated--light and heavy polypeptide chains from an antibody V region into an sFv molecule which will fold into a three dimensional structure substantially similar to the structure of an antigen-binding site. See, e.g., U.S. Pat. Nos. 5,091,513 and 5,132,405, to Huston et al.; and U.S. Pat. No. 4,946,778, to Ladner et al.

Each of the above-described molecules includes a heavy chain and a light chain CDR set, respectively interposed between a heavy chain and a light chain FR set which provide support to the CDRs and define the spatial relationship of the CDRs relative to each other. As used herein, the term "CDR set" refers to the three hypervariable regions of a heavy or light chain V region. Proceeding from the N-terminus of a heavy or light chain, these regions are denoted as "CDR1," "CDR2," and "CDR3" respectively. An antigen-binding site, therefore, includes six CDRs, comprising the CDR set from each of a heavy and a light chain V region. A polypeptide

comprising a single CDR, (e.g., a CDR1, CDR2 or CDR3) is referred to herein as a "molecular recognition unit." Crystallographic analysis of a number of antigen-antibody complexes has demonstrated that the amino acid residues of CDRs form extensive contact with bound antigen, wherein the most extensive antigen contact is with the heavy chain CDR3. Thus, the molecular recognition units are primarily responsible for the specificity of an antigen-binding site.

As used herein, the term "FR set" refers to the four flanking amino acid sequences which frame the CDRs of a CDR set of a heavy or light chain V region. Some FR residues may contact bound antigen; however, FRs are primarily responsible for folding the V region into the antigen-binding site, particularly the FR residues directly adjacent to the CDRs. Within FRs, certain amino residues and certain structural features are very highly conserved. In this regard, all V region sequences contain an internal disulfide loop of around 90 amino acid residues. When the V regions fold into a binding-site, the CDRs are displayed as projecting loop motifs which form an antigen-binding surface. It is generally recognized that there are conserved structural regions of FRs which influence the folded shape of the CDR loops into certain "canonical" structures--regardless of the precise CDR amino acid sequence. Further, certain FR residues are known to participate in non-covalent interdomain contacts which stabilize the interaction of the antibody heavy and light chains.

A number of "humanized" antibody molecules comprising an antigen-binding site derived from a non-human immunoglobulin have been described, including chimeric antibodies having rodent V regions and their associated CDRs fused to human constant domains (Winter et al. (1991) *Nature* 349:293-299; Lobuglio et al. (1989) *Proc. Nat. Acad. Sci. USA* 86:4220-4224; Shaw et al. (1987) *J Immunol.* 138:4534-4538; and Brown et al. (1987) *Cancer Res.* 47:3577-3583), rodent CDRs grafted into a human supporting FR prior to fusion with an appropriate human antibody constant domain (Riechmann et al. (1988) *Nature* 332:323-327; Verhoeven et al. (1988) *Science* 239:1534-1536; and Jones et al. (1986) *Nature* 321:522-525), and rodent CDRs supported by recombinantly veneered rodent FRs (European Patent Publication No. 519,596, published Dec. 23, 1992). These "humanized" molecules are designed to minimize unwanted immunological response toward rodent antihuman antibody

molecules which limits the duration and effectiveness of therapeutic applications of those moieties in human recipients.

As used herein, the terms "veneered FRs" and "recombinantly veneered FRs" refer to the selective replacement of FR residues from, *e.g.*, a rodent heavy or light chain V region, with human FR residues in order to provide a xenogeneic molecule comprising an antigen-binding site which retains substantially all of the native FR polypeptide folding structure. Veneering techniques are based on the understanding that the ligand binding characteristics of an antigen-binding site are determined primarily by the structure and relative disposition of the heavy and light chain CDR sets within the antigen-binding surface. Davies et al. (1990) *Ann. Rev. Biochem.* 59:439-473. Thus, antigen binding specificity can be preserved in a humanized antibody only wherein the CDR structures, their interaction with each other, and their interaction with the rest of the V region domains are carefully maintained. By using veneering techniques, exterior (*e.g.*, solvent-accessible) FR residues which are readily encountered by the immune system are selectively replaced with human residues to provide a hybrid molecule that comprises either a weakly immunogenic, or substantially non-immunogenic veneered surface.

The process of veneering makes use of the available sequence data for human antibody variable domains compiled by Kabat et al., in *Sequences of Proteins of Immunological Interest*, 4th ed., (U.S. Dept. of Health and Human Services, U.S. Government Printing Office, 1987), updates to the Kabat database, and other accessible U.S. and foreign databases (both nucleic acid and protein). Solvent accessibilities of V region amino acids can be deduced from the known three-dimensional structure for human and murine antibody fragments. There are two general steps in veneering a murine antigen-binding site. Initially, the FRs of the variable domains of an antibody molecule of interest are compared with corresponding FR sequences of human variable domains obtained from the above-identified sources. The most homologous human V regions are then compared residue by residue to corresponding murine amino acids. The residues in the murine FR which differ from the human counterpart are replaced by the residues present in the human moiety using recombinant techniques well known in the art. Residue switching is only carried out with moieties which are at least partially

exposed (solvent accessible), and care is exercised in the replacement of amino acid residues which may have a significant effect on the tertiary structure of V region domains, such as proline, glycine and charged amino acids.

In this manner, the resultant "veneered" murine antigen-binding sites are thus designed to retain the murine CDR residues, the residues substantially adjacent to the CDRs, the residues identified as buried or mostly buried (solvent inaccessible), the residues believed to participate in non-covalent (*e.g.*, electrostatic and hydrophobic) contacts between heavy and light chain domains, and the residues from conserved structural regions of the FRs which are believed to influence the "canonical" tertiary structures of the CDR loops. These design criteria are then used to prepare recombinant nucleotide sequences which combine the CDRs of both the heavy and light chain of a murine antigen-binding site into human-appearing FRs that can be used to transfect mammalian cells for the expression of recombinant human antibodies which exhibit the antigen specificity of the murine antibody molecule.

In another embodiment of the invention, monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y , ^{123}I , ^{125}I , ^{131}I , ^{186}Re , ^{188}Re , ^{211}At , and ^{212}Bi . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, Shigella toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid halide, or with an alkyl group containing a good leaving group (*e.g.*, a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an

antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which
5 otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be effected, for example, through amino groups, carboxyl groups,
10 sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, *e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is cleavable during or upon internalization into a cell. A number of
15 different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (*e.g.*, U.S. Patent No. 4,489,710, to Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by
20 serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody.
25 Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers that provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent
30 bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides

such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

T Cell Compositions

The present invention, in another aspect, provides T cells specific for a tumor polypeptide disclosed herein, or for a variant or derivative thereof. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the Isolex™ System, available from Nexell Therapeutics, Inc. (Irvine, CA; see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a polypeptide, polynucleotide encoding a polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide of interest. Preferably, a tumor polypeptide or polynucleotide of the invention is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a polypeptide of the present invention if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a variety of standard techniques. For

example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* 54:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell proliferation can be detected by measuring an increased rate of DNA synthesis (e.g., by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a tumor polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days will typically result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (e.g., TNF or IFN-γ) is indicative of T cell activation (see Coligan et al., *Current Protocols in Immunology*, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a tumor polypeptide, polynucleotide or polypeptide-expressing APC may be CD4⁺ and/or CD8⁺. Tumor polypeptide-specific T cells may be expanded using standard techniques. Within preferred embodiments, the T cells are derived from a patient, a related donor or an unrelated donor, and are administered to the patient following stimulation and expansion.

For therapeutic purposes, CD4⁺ or CD8⁺ T cells that proliferate in response to a tumor polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a tumor polypeptide, or a short peptide corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a tumor polypeptide. Alternatively, one or more T cells that proliferate in the presence of the tumor polypeptide can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

T Cell Receptor Compositions

The T cell receptor (TCR) consists of 2 different, highly variable polypeptide chains, termed the T-cell receptor α and β chains, that are linked by a disulfide bond (Janeway, Travers, Walport. *Immunobiology*. Fourth Ed., 148-159. Elsevier Science Ltd/Garland Publishing. 1999). The α/β heterodimer complexes with the invariant CD3 chains at the cell membrane. This complex recognizes specific antigenic peptides bound to MHC molecules. The enormous diversity of TCR specificities is generated much like immunoglobulin diversity, through somatic gene rearrangement. The β chain genes contain over 50 variable (V), 2 diversity (D), over 10 joining (J) segments, and 2 constant region segments (C). The α chain genes contain over 70 V segments, and over 60 J segments but no D segments, as well as one C segment. During T cell development in the thymus, the D to J gene rearrangement of the β chain occurs, followed by the V gene segment rearrangement to the DJ. This functional VDJ β exon is transcribed and spliced to join to a C β . For the α chain, a V α gene segment rearranges to a J α gene segment to create the functional exon that is then transcribed and spliced to the C α . Diversity is further increased during the recombination process by the random addition of P and N-nucleotides between the V, D, and J segments of the β chain and between the V and J segments in the α chain (Janeway, Travers, Walport. *Immunobiology*. Fourth Ed., 98 and 150. Elsevier Science Ltd/Garland Publishing. 1999).

The present invention, in another aspect, provides TCRs specific for a polypeptide disclosed herein, or for a variant or derivative thereof. In accordance with the present invention, polynucleotide and amino acid sequences are provided for the V-J or V-D-J junctional regions or parts thereof for the alpha and beta chains of the T-cell receptor which recognize tumor polypeptides described herein. In general, this aspect of the invention relates to T-cell receptors which recognize or bind tumor polypeptides presented in the context of MHC. In a preferred embodiment the tumor antigens recognized by the T-cell receptors comprise a polypeptide of the present invention. For example, cDNA encoding a TCR specific for a _tumor peptide can be isolated from T cells specific for a tumor polypeptide using standard molecular biological and recombinant DNA techniques.

This invention further includes the T-cell receptors or analogs thereof having substantially the same function or activity as the T-cell receptors of this invention which recognize or bind tumor polypeptides. Such receptors include, but are not limited to, a fragment of the receptor, or a substitution, addition or deletion mutant of a T-cell receptor provided herein. This invention also encompasses polypeptides or peptides that are substantially homologous to the T-cell receptors provided herein or that retain substantially the same activity. The term "analog" includes any protein or polypeptide having an amino acid residue sequence substantially identical to the T-cell receptors provided herein in which one or more residues, preferably no more than 5 residues, more preferably no more than 25 residues have been conservatively substituted with a functionally similar residue and which displays the functional aspects of the T-cell receptor as described herein.

The present invention further provides for suitable mammalian host cells, for example, non-specific T cells, that are transfected with a polynucleotide encoding TCRs specific for a polypeptide described herein, thereby rendering the host cell specific for the polypeptide. The α and β chains of the TCR may be contained on separate expression vectors or alternatively, on a single expression vector that also contains an internal ribosome entry site (IRES) for cap-independent translation of the gene downstream of the IRES. Said host cells expressing TCRs specific for the polypeptide may be used, for example, for adoptive immunotherapy of lung cancer as discussed further below.

In further aspects of the present invention, cloned TCRs specific for a polypeptide recited herein may be used in a kit for the diagnosis of lung cancer. For example, the nucleic acid sequence or portions thereof, of tumor-specific TCRs can be used as probes or primers for the detection of expression of the rearranged genes encoding the specific TCR in a biological sample. Therefore, the present invention further provides for an assay for detecting messenger RNA or DNA encoding the TCR specific for a polypeptide.

Pharmaceutical Compositions

In additional embodiments, the present invention concerns formulation of one or more of the polynucleotide, polypeptide, T-cell and/or antibody compositions disclosed herein in pharmaceutically-acceptable carriers for administration to a cell or an animal, either alone, or in combination with one or more other modalities of therapy.

It will be understood that, if desired, a composition as disclosed herein may be administered in combination with other agents as well, such as, *e.g.*, other proteins or polypeptides or various pharmaceutically-active agents. In fact, there is virtually no limit to other components that may also be included, given that the additional agents do not cause a significant adverse effect upon contact with the target cells or host tissues. The compositions may thus be delivered along with various other agents as required in the particular instance. Such compositions may be purified from host cells or other biological sources, or alternatively may be chemically synthesized as described herein. Likewise, such compositions may further comprise substituted or derivatized RNA or DNA compositions.

Therefore, in another aspect of the present invention, pharmaceutical compositions are provided comprising one or more of the polynucleotide, polypeptide, antibody, and/or T-cell compositions described herein in combination with a physiologically acceptable carrier. In certain preferred embodiments, the pharmaceutical compositions of the invention comprise immunogenic polynucleotide and/or polypeptide compositions of the invention for use in prophylactic and therapeutic vaccine applications. Vaccine preparation is generally described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Generally, such compositions will comprise one or more polynucleotide and/or polypeptide compositions of the present invention in combination with one or more immunostimulants.

It will be apparent that any of the pharmaceutical compositions described herein can contain pharmaceutically acceptable salts of the polynucleotides and polypeptides of the invention. Such salts can be prepared, for example, from pharmaceutically acceptable non-toxic bases, including organic bases (*e.g.*, salts of

primary, secondary and tertiary amines and basic amino acids) and inorganic bases (e.g., sodium, potassium, lithium, ammonium, calcium and magnesium salts).

- In another embodiment, illustrative immunogenic compositions, e.g., vaccine compositions, of the present invention comprise DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the polynucleotide may be administered within any of a variety of delivery systems known to those of ordinary skill in the art. Indeed, numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems* 15:143-198, 1998, and references cited therein.
- Appropriate polynucleotide expression systems will, of course, contain the necessary regulatory DNA regulatory sequences for expression in a patient (such as a suitable promoter and terminating signal). Alternatively, bacterial delivery systems may involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope.
- Therefore, in certain embodiments, polynucleotides encoding immunogenic polypeptides described herein are introduced into suitable mammalian host cells for expression using any of a number of known viral-based systems. In one illustrative embodiment, retroviruses provide a convenient and effective platform for gene delivery systems. A selected nucleotide sequence encoding a polypeptide of the present invention can be inserted into a vector and packaged in retroviral particles using techniques known in the art. The recombinant virus can then be isolated and delivered to a subject. A number of illustrative retroviral systems have been described (e.g., U.S. Pat. No. 5,219,740; Miller and Rosman (1989) *BioTechniques* 7:980-990; Miller, A. D. (1990) *Human Gene Therapy* 1:5-14; Scarpa et al. (1991) *Virology* 180:849-852; Burns et al. (1993) *Proc. Natl. Acad. Sci. USA* 90:8033-8037; and Boris-Lawrie and Temin (1993) *Cur. Opin. Genet. Develop.* 3:102-109.

- In addition, a number of illustrative adenovirus-based systems have also been described. Unlike retroviruses which integrate into the host genome, adenoviruses persist extrachromosomally thus minimizing the risks associated with insertional mutagenesis (Haj-Ahmad and Graham (1986) *J. Virol.* 57:267-274; Bett et al. (1993) *J. Virol.* 67:5911-5921; Mittereder et al. (1994) *Human Gene Therapy* 5:717-729; Seth et

al. (1994) *J. Virol.* 68:933-940; Barr et al. (1994) *Gene Therapy* 1:51-58; Berkner, K. L. (1988) *BioTechniques* 6:616-629; and Rich et al. (1993) *Human Gene Therapy* 4:461-476).

Various adeno-associated virus (AAV) vector systems have also been
5 developed for polynucleotide delivery. AAV vectors can be readily constructed using
techniques well known in the art. See, e.g., U.S. Pat. Nos. 5,173,414 and 5,139,941;
International Publication Nos. WO 92/01070 and WO 93/03769; Lebkowski et al.
(1988) *Molec. Cell. Biol.* 8:3988-3996; Vincent et al. (1990) *Vaccines 90* (Cold Spring
Harbor Laboratory Press); Carter, B. J. (1992) *Current Opinion in Biotechnology* 3:533-
10 539; Muzyczka, N. (1992) *Current Topics in Microbiol. and Immunol.* 158:97-129;
Kotin, R. M. (1994) *Human Gene Therapy* 5:793-801; Shelling and Smith (1994) *Gene
Therapy* 1:165-169; and Zhou et al. (1994) *J. Exp. Med.* 179:1867-1875.

Additional viral vectors useful for delivering the polynucleotides
encoding polypeptides of the present invention by gene transfer include those derived
15 from the pox family of viruses, such as vaccinia virus and avian poxvirus. By way of
example, vaccinia virus recombinants expressing the novel molecules can be
constructed as follows. The DNA encoding a polypeptide is first inserted into an
appropriate vector so that it is adjacent to a vaccinia promoter and flanking vaccinia
DNA sequences, such as the sequence encoding thymidine kinase (TK). This vector is
20 then used to transfect cells which are simultaneously infected with vaccinia.
Homologous recombination serves to insert the vaccinia promoter plus the gene
encoding the polypeptide of interest into the viral genome. The resulting TK.sup.(-)
recombinant can be selected by culturing the cells in the presence of 5-
bromodeoxyuridine and picking viral plaques resistant thereto.

25 A vaccinia-based infection/transfection system can be conveniently used
to provide for inducible, transient expression or coexpression of one or more
polypeptides described herein in host cells of an organism. In this particular system,
cells are first infected in vitro with a vaccinia virus recombinant that encodes the
bacteriophage T7 RNA polymerase. This polymerase displays exquisite specificity in
30 that it only transcribes templates bearing T7 promoters. Following infection, cells are
transfected with the polynucleotide or polynucleotides of interest, driven by a T7

promoter. The polymerase expressed in the cytoplasm from the vaccinia virus recombinant transcribes the transfected DNA into RNA which is then translated into polypeptide by the host translational machinery. The method provides for high level, transient, cytoplasmic production of large quantities of RNA and its translation products. See, e.g., Elroy-Stein and Moss, *Proc. Natl. Acad. Sci. USA* (1990) 87:6743-6747; Fuerst et al. *Proc. Natl. Acad. Sci. USA* (1986) 83:8122-8126.

Alternatively, avipoxviruses, such as the fowlpox and canarypox viruses, can also be used to deliver the coding sequences of interest. Recombinant avipox viruses, expressing immunogens from mammalian pathogens, are known to confer protective immunity when administered to non-avian species. The use of an Avipox vector is particularly desirable in human and other mammalian species since members of the Avipox genus can only productively replicate in susceptible avian species and therefore are not infective in mammalian cells. Methods for producing recombinant Avipoxviruses are known in the art and employ genetic recombination, as described above with respect to the production of vaccinia viruses. See, e.g., WO 91/12882; WO 89/03429; and WO 92/03545.

Any of a number of alphavirus vectors can also be used for delivery of polynucleotide compositions of the present invention, such as those vectors described in U.S. Patent Nos. 5,843,723; 6,015,686; 6,008,035 and 6,015,694. Certain vectors based on Venezuelan Equine Encephalitis (VEE) can also be used, illustrative examples of which can be found in U.S. Patent Nos. 5,505,947 and 5,643,576.

Moreover, molecular conjugate vectors, such as the adenovirus chimeric vectors described in Michael et al. *J. Biol. Chem.* (1993) 268:6866-6869 and Wagner et al. *Proc. Natl. Acad. Sci. USA* (1992) 89:6099-6103, can also be used for gene delivery under the invention.

Additional illustrative information on these and other known viral-based delivery systems can be found, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA* 86:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci.* 569:86-103, 1989; Flexner et al., *Vaccine* 8:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242; WO 91/02805; Berkner, *Biotechniques* 6:616-627, 1988; Rosenfeld et al., *Science*

252:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA* 91:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA* 90:11498-11502, 1993; Guzman et al., *Circulation* 88:2838-2848, 1993; and Guzman et al., *Cir. Res.* 73:1202-1207, 1993.

In certain embodiments, a polynucleotide may be integrated into the
5 genome of a target cell. This integration may be in the specific location and orientation
via homologous recombination (gene replacement) or it may be integrated in a random,
non-specific location (gene augmentation). In yet further embodiments, the
polynucleotide may be stably maintained in the cell as a separate, episomal segment of
DNA. Such polynucleotide segments or "episomes" encode sequences sufficient to
10 permit maintenance and replication independent of or in synchronization with the host
cell cycle. The manner in which the expression construct is delivered to a cell and
where in the cell the polynucleotide remains is dependent on the type of expression
construct employed.

In another embodiment of the invention, a polynucleotide is
15 administered/delivered as "naked" DNA, for example as described in Ulmer et al.,
Science 259:1745-1749, 1993 and reviewed by Cohen, *Science* 259:1691-1692, 1993.
The uptake of naked DNA may be increased by coating the DNA onto biodegradable
beads, which are efficiently transported into the cells.

In still another embodiment, a composition of the present invention can
20 be delivered via a particle bombardment approach, many of which have been described.
In one illustrative example, gas-driven particle acceleration can be achieved with
devices such as those manufactured by Powderject Pharmaceuticals PLC (Oxford, UK)
and Powderject Vaccines Inc. (Madison, WI), some examples of which are described in
U.S. Patent Nos. 5,846,796; 6,010,478; 5,865,796; 5,584,807; and EP Patent No. 0500
25 799. This approach offers a needle-free delivery approach wherein a dry powder
formulation of microscopic particles, such as polynucleotide or polypeptide particles,
are accelerated to high speed within a helium gas jet generated by a hand held device,
propelling the particles into a target tissue of interest.

In a related embodiment, other devices and methods that may be useful
30 for gas-driven needle-less injection of compositions of the present invention include
those provided by Bioject, Inc. (Portland, OR), some examples of which are described

in U.S. Patent Nos. 4,790,824; 5,064,413; 5,312,335; 5,383,851; 5,399,163; 5,520,639 and 5,993,412.

According to another embodiment, the pharmaceutical compositions described herein will comprise one or more immunostimulants in addition to the immunogenic polynucleotide, polypeptide, antibody, T-cell and/or APC compositions of this invention. An immunostimulant refers to essentially any substance that enhances or potentiates an immune response (antibody and/or cell-mediated) to an exogenous antigen. One preferred type of immunostimulant comprises an adjuvant. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bordetella pertussis* or *Mycobacterium tuberculosis* derived proteins. Certain adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Within certain embodiments of the invention, the adjuvant composition is preferably one that induces an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (e.g., IFN- γ , TNF α , IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (e.g., IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2-type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using

standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Certain preferred adjuvants for eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A, together with an aluminum salt. MPL®
5 adjuvants are available from Corixa Corporation (Seattle, WA; *see*, for example, US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described,
10 for example, in WO 96/02555, WO 99/33488 and U.S. Patent Nos. 6,008,200 and 5,856,462. Immunostimulatory DNA sequences are also described, for example, by Sato et al., *Science* 273:352, 1996. Another preferred adjuvant comprises a saponin, such as Quil A, or derivatives thereof, including QS21 and QS7 (Aquila Biopharmaceuticals Inc., Framingham, MA); Escin; Digitonin; or *Gypsophila* or
15 *Chenopodium quinoa* saponins. Other preferred formulations include more than one saponin in the adjuvant combinations of the present invention, for example combinations of at least two of the following group comprising QS21, QS7, Quil A, β -escin, or digitonin.

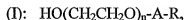
Alternatively the saponin formulations may be combined with vaccine
20 vehicles composed of chitosan or other polycationic polymers, polylactide and polylactide-co-glycolide particles, poly-N-acetyl glucosamine-based polymer matrix, particles composed of polysaccharides or chemically modified polysaccharides, liposomes and lipid-based particles, particles composed of glycerol monoesters, etc. The saponins may also be formulated in the presence of cholesterol to form particulate
25 structures such as liposomes or ISCOMs. Furthermore, the saponins may be formulated together with a polyoxyethylene ether or ester, in either a non-particulate solution or suspension, or in a particulate structure such as a paucilamellar liposome or ISCOM. The saponins may also be formulated with excipients such as Carbopol® to increase viscosity, or may be formulated in a dry powder form with a powder excipient such as
30 lactose.

In one preferred embodiment, the adjuvant system includes the combination of a monophosphoryl lipid A and a saponin derivative, such as the combination of QS21 and 3D-MPL[®] adjuvant, as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in
5 WO 96/33739. Other preferred formulations comprise an oil-in-water emulsion and tocopherol. Another particularly preferred adjuvant formulation employing QS21, 3D-MPL[®] adjuvant and tocopherol in an oil-in-water emulsion is described in WO 95/17210.

Another enhanced adjuvant system involves the combination of a CpG-
10 containing oligonucleotide and a saponin derivative particularly the combination of CpG and QS21 is disclosed in WO 00/09159. Preferably the formulation additionally comprises an oil in water emulsion and tocopherol.

Additional illustrative adjuvants for use in the pharmaceutical compositions of the invention include Montanide ISA 720 (Seppic, France), SAF
15 (Chiron, California, United States), ISCOMS (CSL), MF-59 (Chiron), the SBAS series of adjuvants (*e.g.*, SBAS-2 or SBAS-4, available from SmithKline Beecham, Rixensart, Belgium), Detox (Enhanzyn[®]) (Corixa, Hamilton, MT), RC-529 (Corixa, Hamilton, MT) and other aminoalkyl glucosaminide 4-phosphates (AGPs), such as those described in pending U.S. Patent Application Serial Nos. 08/853,826 and 09/074,720, the
20 disclosures of which are incorporated herein by reference in their entireties, and polyoxyethylene ether adjuvants such as those described in WO 99/52549A1.

Other preferred adjuvants include adjuvant molecules of the general formula



25 wherein, n is 1-50, A is a bond or $-\text{C}(\text{O})-$, R is C_{1-50} alkyl or Phenyl C_{1-50} alkyl.

One embodiment of the present invention consists of a vaccine formulation comprising a polyoxyethylene ether of general formula (I), wherein n is between 1 and 50, preferably 4-24, most preferably 9; the R component is C_{1-50} , preferably $\text{C}_4\text{-C}_{20}$ alkyl and most preferably C_{12} alkyl, and A is a bond. The
30 concentration of the polyoxyethylene ethers should be in the range 0.1-20%, preferably from 0.1-10%, and most preferably in the range 0.1-1%. Preferred polyoxyethylene

ethers are selected from the following group: polyoxyethylene-9-lauryl ether, polyoxyethylene-9-stearyl ether, polyoxyethylene-8-stearyl ether, polyoxyethylene-4-lauryl ether, polyoxyethylene-35-lauryl ether, and polyoxyethylene-23-lauryl ether. Polyoxyethylene ethers such as polyoxyethylene lauryl ether are described in the Merck index (12th edition: entry 7717). These adjuvant molecules are described in WO 99/52549.

The polyoxyethylene ether according to the general formula (I) above may, if desired, be combined with another adjuvant. For example, a preferred adjuvant combination is preferably with CpG as described in the pending UK patent application GB 9820956.2.

According to another embodiment of this invention, an immunogenic composition described herein is delivered to a host via antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature* 392:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy, *Ann. Rev. Med.* 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take up, process and present antigens with high efficiency and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As

an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med.* 4:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNF α to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNF α , CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fc γ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II MHC, adhesion molecules (*e.g.*, CD54 and CD11) and costimulatory molecules (*e.g.*, CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide of the invention (or portion or other variant thereof) such that the encoded polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex vivo*, and a pharmaceutical composition comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any

methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology* 75:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells with the tumor polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (e.g., vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (e.g., a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of the polypeptide.

- 10 While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will typically vary depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, mucosal, intravenous, intracranial, 15 intraperitoneal, subcutaneous and intramuscular administration.

- Carriers for use within such pharmaceutical compositions are biocompatible, and may also be biodegradable. In certain embodiments, the formulation preferably provides a relatively constant level of active component release. In other embodiments, however, a more rapid rate of release immediately upon 20 administration may be desired. The formulation of such compositions is well within the level of ordinary skill in the art using known techniques. Illustrative carriers useful in this regard include microparticles of poly(lactide-co-glycolide), polyacrylate, latex, starch, cellulose, dextran and the like. Other illustrative delayed-release carriers include supramolecular biovectors, which comprise a non-liquid hydrophilic core (e.g., 25 a cross-linked polysaccharide or oligosaccharide) and, optionally, an external layer comprising an amphiphilic compound, such as a phospholipid (see e.g., U.S. Patent No. 5,151,254 and PCT applications WO 94/20078, WO/94/23701 and WO 96/06638). The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of 30 the condition to be treated or prevented.

In another illustrative embodiment, biodegradable microspheres (*e.g.*, polylactate polyglycolate) are employed as carriers for the compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268; 5,075,109; 5,928,647; 5,811,128; 5,820,883; 5,853,763; 5,814,344, 5,407,609 and 5,942,252. Modified hepatitis B core protein carrier systems, such as described in WO/99 40934, and references cited therein, will also be useful for many applications. Another illustrative carrier/delivery system employs a carrier comprising particulate-protein complexes, such as those described in U.S. Patent No. 5,928,647, which are capable of inducing a class I-restricted cytotoxic T lymphocyte responses in a host.

The pharmaceutical compositions of the invention will often further comprise one or more buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, bacteriostats, chelating agents such as EDTA or glutathione, adjuvants (*e.g.*, aluminum hydroxide), solutes that render the formulation isotonic, hypotonic or weakly hypertonic with the blood of a recipient, suspending agents, thickening agents and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate.

The pharmaceutical compositions described herein may be presented in unit-dose or multi-dose containers, such as sealed ampoules or vials. Such containers are typically sealed in such a way to preserve the sterility and stability of the formulation until use. In general, formulations may be stored as suspensions, solutions or emulsions in oily or aqueous vehicles. Alternatively, a pharmaceutical composition may be stored in a freeze-dried condition requiring only the addition of a sterile liquid carrier immediately prior to use.

The development of suitable dosing and treatment regimens for using the particular compositions described herein in a variety of treatment regimens, including *e.g.*, oral, parenteral, intravenous, intranasal, and intramuscular administration and formulation, is well known in the art, some of which are briefly discussed below for general purposes of illustration.

In certain applications, the pharmaceutical compositions disclosed herein may be delivered *via* oral administration to an animal. As such, these compositions may be formulated with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard- or soft-shell gelatin capsule, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet.

The active compounds may even be incorporated with excipients and used in the form of ingestible tablets, buccal tables, troches, capsules, elixirs, suspensions, syrups, wafers, and the like (see, for example, Mathiowitz *et al.*, Nature 1997 Mar 27;386(6623):410-4; Hwang *et al.*, Crit Rev Ther Drug Carrier Syst 1998;15(3):243-84; U. S. Patent 5,641,515; U. S. Patent 5,580,579 and U. S. Patent 5,792,451). Tablets, troches, pills, capsules and the like may also contain any of a variety of additional components, for example, a binder, such as gum tragacanth, acacia, cornstarch, or gelatin; excipients, such as dicalcium phosphate; a disintegrating agent, such as corn starch, potato starch, alginic acid and the like; a lubricant, such as magnesium stearate; and a sweetening agent, such as sucrose, lactose or saccharin may be added or a flavoring agent, such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar, or both. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparation and formulations.

Typically, these formulations will contain at least about 0.1% of the active compound or more, although the percentage of the active ingredient(s) may, of course, be varied and may conveniently be between about 1 or 2% and about 60% or 70% or more of the weight or volume of the total formulation. Naturally, the amount of active compound(s) in each therapeutically useful composition may be prepared is such a way that a suitable dosage will be obtained in any given unit dose of the compound. Factors such as solubility, bioavailability, biological half-life, route of administration, product shelf life, as well as other pharmacological considerations will be contemplated

by one skilled in the art of preparing such pharmaceutical formulations, and as such, a variety of dosages and treatment regimens may be desirable.

For oral administration the compositions of the present invention may alternatively be incorporated with one or more excipients in the form of a mouthwash, dentifrice, buccal tablet, oral spray, or sublingual orally-administered formulation. Alternatively, the active ingredient may be incorporated into an oral solution such as one containing sodium borate, glycerin and potassium bicarbonate, or dispersed in a dentifrice, or added in a therapeutically-effective amount to a composition that may include water, binders, abrasives, flavoring agents, foaming agents, and humectants. Alternatively the compositions may be fashioned into a tablet or solution form that may be placed under the tongue or otherwise dissolved in the mouth.

In certain circumstances it will be desirable to deliver the pharmaceutical compositions disclosed herein parenterally, intravenously, intramuscularly, or even intraperitoneally. Such approaches are well known to the skilled artisan, some of which are further described, for example, in U. S. Patent 5,543,158; U. S. Patent 5,641,515 and U. S. Patent 5,399,363. In certain embodiments, solutions of the active compounds as free base or pharmacologically acceptable salts may be prepared in water suitably mixed with a surfactant, such as hydroxypropylcellulose. Dispersions may also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations generally will contain a preservative to prevent the growth of microorganisms.

Illustrative pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporaneous preparation of sterile injectable solutions or dispersions (for example, see U. S. Patent 5,466,468). In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms, such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (e.g., glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and/or vegetable oils. Proper fluidity may be maintained, for example, by the use of a coating, such as

lecithin, by the maintenance of the required particle size in the case of dispersion and/or by the use of surfactants. The prevention of the action of microorganisms can be facilitated by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

In one embodiment, for parenteral administration in an aqueous solution, the solution should be suitably buffered if necessary and the liquid diluent first rendered isotonic with sufficient saline or glucose. These particular aqueous solutions are especially suitable for intravenous, intramuscular, subcutaneous and intraperitoneal administration. In this connection, a sterile aqueous medium that can be employed will be known to those of skill in the art in light of the present disclosure. For example, one dosage may be dissolved in 1 ml of isotonic NaCl solution and either added to 1000 ml of hypodermoclysis fluid or injected at the proposed site of infusion, (see for example, "Remington's Pharmaceutical Sciences" 15th Edition, pages 1035-1038 and 1570-1580). Some variation in dosage will necessarily occur depending on the condition of the subject being treated. Moreover, for human administration, preparations will of course preferably meet sterility, pyrogenicity, and the general safety and purity standards as required by FDA Office of Biologics standards.

In another embodiment of the invention, the compositions disclosed herein may be formulated in a neutral or salt form. Illustrative pharmaceutically-acceptable salts include the acid addition salts (formed with the free amino groups of the protein) and which are formed with inorganic acids such as, for example, hydrochloric or phosphoric acids, or such organic acids as acetic, oxalic, tartaric, mandelic, and the like. Salts formed with the free carboxyl groups can also be derived from inorganic bases such as, for example, sodium, potassium, ammonium, calcium, or ferric hydroxides, and such organic bases as isopropylamine, trimethylamine, histidine, procaine and the like. Upon formulation, solutions will be

administered in a manner compatible with the dosage formulation and in such amount as is therapeutically effective.

The carriers can further comprise any and all solvents, dispersion media, vehicles, coatings, diluents, antibacterial and antifungal agents, isotonic and absorption
5 delaying agents, buffers, carrier solutions, suspensions, colloids, and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. The phrase
10 "pharmaceutically-acceptable" refers to molecular entities and compositions that do not produce an allergic or similar untoward reaction when administered to a human.

In certain embodiments, the pharmaceutical compositions may be delivered by intranasal sprays, inhalation, and/or other aerosol delivery vehicles. Methods for delivering genes, nucleic acids, and peptide compositions directly to the
15 lungs *via* nasal aerosol sprays has been described, *e.g.*, in U. S. Patent 5,756,353 and U. S. Patent 5,804,212. Likewise, the delivery of drugs using intranasal microparticle resins (Takenaga *et al.*, J Controlled Release 1998 Mar 2;52(1-2):81-7) and lysophosphatidyl-glycerol compounds (U. S. Patent 5,725,871) are also well-known in the pharmaceutical arts. Likewise, illustrative transmucosal drug delivery in the form of
20 a polytetrafluoroethylene support matrix is described in U. S. Patent 5,780,045.

In certain embodiments, liposomes, nanocapsules, microparticles, lipid particles, vesicles, and the like, are used for the introduction of the compositions of the present invention into suitable host cells/organisms. In particular, the compositions of the present invention may be formulated for delivery either encapsulated in a lipid
25 particle, a liposome, a vesicle, a nanosphere, or a nanoparticle or the like. Alternatively, compositions of the present invention can be bound, either covalently or non-covalently, to the surface of such carrier vehicles.

The formation and use of liposome and liposome-like preparations as potential drug carriers is generally known to those of skill in the art (see for example,
30 Lasic, Trends Biotechnol 1998 Jul;16(7):307-21; Takakura, Nippon Rinsho 1998 Mar;56(3):691-5; Chandran *et al.*, Indian J Exp Biol. 1997 Aug;35(8):801-9; Margalit,

Crit Rev Ther Drug Carrier Syst. 1995;12(2-3):233-61; U.S. Patent 5,567,434; U.S. Patent 5,552,157; U.S. Patent 5,565,213; U.S. Patent 5,738,868 and U.S. Patent 5,795,587, each specifically incorporated herein by reference in its entirety).

Liposomes have been used successfully with a number of cell types that are normally difficult to transfect by other procedures, including T cell suspensions, primary hepatocyte cultures and PC 12 cells (Renneisen *et al.*, J Biol Chem. 1990 Sep 25;265(27):16337-42; Muller *et al.*, DNA Cell Biol. 1990 Apr;9(3):221-9). In addition, liposomes are free of the DNA length constraints that are typical of viral-based delivery systems. Liposomes have been used effectively to introduce genes, various drugs, radiotherapeutic agents, enzymes, viruses, transcription factors, allosteric effectors and the like, into a variety of cultured cell lines and animals. Furthermore, the use of liposomes does not appear to be associated with autoimmune responses or unacceptable toxicity after systemic delivery.

In certain embodiments, liposomes are formed from phospholipids that are dispersed in an aqueous medium and spontaneously form multilamellar concentric bilayer vesicles (also termed multilamellar vesicles (MLVs)).

Alternatively, in other embodiments, the invention provides for pharmaceutically-acceptable nanocapsule formulations of the compositions of the present invention. Nanocapsules can generally entrap compounds in a stable and reproducible way (see, for example, Quintanar-Guerrero *et al.*, Drug Dev Ind Pharm. 1998 Dec;24(12):1113-28). To avoid side effects due to intracellular polymeric overloading, such ultrafine particles (sized around 0.1 μm) may be designed using polymers able to be degraded *in vivo*. Such particles can be made as described, for example, by Couvreur *et al.*, Crit Rev Ther Drug Carrier Syst. 1988;5(1):1-20; zur Muhlen *et al.*, Eur J Pharm Biopharm. 1998 Mar;45(2):149-55; Zambaux *et al.* J Controlled Release. 1998 Jan 2;50(1-3):31-40; and U. S. Patent 5,145,684.

Cancer Therapeutic Methods

Immunologic approaches to cancer therapy are based on the recognition that cancer cells can often evade the body's defenses against aberrant or foreign cells and molecules, and that these defenses might be therapeutically stimulated to regain the

lost ground, *e.g.* pgs. 623-648 in Klein, Immunology (Wiley-Interscience, New York, 1982). Numerous recent observations that various immune effectors can directly or indirectly inhibit growth of tumors has led to renewed interest in this approach to cancer therapy, *e.g.* Jager, et al., Oncology 2001;60(1):1-7; Renner, et al., Ann Hematol 2000

5 Dec;79(12):651-9.

Four-basic cell types whose function has been associated with antitumor cell immunity and the elimination of tumor cells from the body are: i) B-lymphocytes which secrete immunoglobulins into the blood plasma for identifying and labeling the nonself invader cells; ii) monocytes which secrete the complement proteins that are
10 responsible for lysing and processing the immunoglobulin-coated target invader cells; iii) natural killer lymphocytes having two mechanisms for the destruction of tumor cells, antibody-dependent cellular cytotoxicity and natural killing; and iv) T-lymphocytes possessing antigen-specific receptors and having the capacity to recognize a tumor cell carrying complementary marker molecules (Schreiber, H., 1989, in
15 Fundamental Immunology (ed). W. E. Paul, pp. 923-955).

Cancer immunotherapy generally focuses on inducing humoral immune responses, cellular immune responses, or both. Moreover, it is well established that induction of CD4⁺ T helper cells is necessary in order to secondarily induce either antibodies or cytotoxic CD8⁺ T cells. Polypeptide antigens that are selective or ideally
20 specific for cancer cells, particularly lung cancer cells, offer a powerful approach for inducing immune responses against lung cancer, and are an important aspect of the present invention.

Therefore, in further aspects of the present invention, the pharmaceutical compositions described herein may be used for the treatment of cancer, particularly for
25 the immunotherapy of lung cancer. Within such methods, the pharmaceutical compositions described herein are administered to a patient, typically a warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. Pharmaceutical
30 compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or

conventional chemotherapeutic drugs. As discussed above, administration of the pharmaceutical compositions may be by any suitable method, including administration by intravenous, intraperitoneal, intramuscular, subcutaneous, intranasal, intradermal, anal, vaginal, topical and oral routes.

5 Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides as provided herein).

10 Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T
15 lymphocytes (such as CD8⁺ cytotoxic T lymphocytes and CD4⁺ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody
20 receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

 Monoclonal antibodies may be labeled with any of a variety of labels for
25 desired selective usages in detection, diagnostic assays or therapeutic applications (as described in U.S. Patent Nos. 6,090,365; 6,015,542; 5,843,398; 5,595,721; and 4,708,930, hereby incorporated by reference in their entirety as if each was incorporated individually). In each case, the binding of the labelled monoclonal antibody to the
determinant site of the antigen will signal detection or delivery of a particular
30 therapeutic agent to the antigenic determinant on the non-normal cell. A further object

of this invention is to provide the specific monoclonal antibody suitably labelled for achieving such desired selective usages thereof.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte, fibroblast and/or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies have shown that cultured effector cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews* 157:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions described herein, as well as dosage, will vary from individual to individual, and may be readily established using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered over a 52 week period.

Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50% above the basal (*i.e.*, untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells *in vitro*. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 µg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (*e.g.*, more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a tumor protein generally correlate with an improved clinical outcome. Such immune responses may generally be evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

Cancer Detection and Diagnostic Compositions, Methods and Kits

In general, a cancer may be detected in a patient based on the presence of one or more lung tumor proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, sputum urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as lung cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided

herein generally permit detection of the level of antigen that binds to the agent in the biological sample.

Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer. In general, a tumor sequence should be present at a level that is at least two-fold, preferably three-fold, and more preferably five-fold or higher in tumor tissue than in normal tissue of the same type from which the tumor arose. Expression levels of a particular tumor sequence in tissue types different from that in which the tumor arose are irrelevant in certain diagnostic embodiments since the presence of tumor cells can be confirmed by observation of predetermined differential expression levels, e.g., 2-fold, 5-fold, etc, in tumor tissue to expression levels in normal tissue of the same type.

Other differential expression patterns can be utilized advantageously for diagnostic purposes. For example, in one aspect of the invention, overexpression of a tumor sequence in tumor tissue and normal tissue of the same type, but not in other normal tissue types, e.g. PBMCs, can be exploited diagnostically. In this case, the presence of metastatic tumor cells, for example in a sample taken from the circulation or some other tissue site different from that in which the tumor arose, can be identified and/or confirmed by detecting expression of the tumor sequence in the sample, for example using RT-PCR analysis. In many instances, it will be desired to enrich for tumor cells in the sample of interest, e.g., PBMCs, using cell capture or other like techniques.

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. See, e.g., Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection

reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,
5 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding
10 agent. Suitable polypeptides for use within such assays include full length lung tumor proteins and polypeptide portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the tumor protein may be attached. For example, the solid support
15 may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support
20 using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent).
25 Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or
30 polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about

10 μg , and preferably about 100 ng to about 1 μg , is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with
5 both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.*, Pierce Immunotechnology Catalog and Handbook, 1991, at
10 A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody.
15 Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

20 More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20TM (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to
25 bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (*i.e.*, incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with lung cancer. Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of
30 that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium

may be readily determined by assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support
5 with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide.
10 An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally
15 appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction
20 products.

To determine the presence or absence of a cancer, such as lung cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average
25 mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical*
30 *Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot

of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a
5 signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

10 In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution
15 containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent.
20 Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the
25 biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1 μ g, and more preferably from about 50 ng to about
30 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the tumor proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use
5 tumor polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such tumor protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a tumor protein in a biological sample. Within
10 certain methods, a biological sample comprising CD4⁺ and/or CD8⁺ T cells isolated from a patient is incubated with a tumor polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For
15 example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with polypeptide (e.g., 5 - 25 µg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of tumor polypeptide to serve as a control. For CD4⁺ T cells, activation is
20 preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on
25 the level of mRNA encoding a tumor protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify a portion of a tumor cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the tumor protein. The amplified cDNA is
30 then separated and detected using techniques well known in the art, such as gel electrophoresis.

Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a tumor protein may be used in a hybridization assay to detect the presence of polynucleotide encoding the tumor protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a tumor protein of the invention that is at least 10 nucleotides, and preferably at least 20 nucleotides, in length. Preferably, oligonucleotide primers and/or probes hybridize to a polynucleotide encoding a polypeptide described herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15 contiguous nucleotides, of a DNA molecule having a sequence as disclosed herein. Techniques for both PCR based assays and hybridization assays are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, 51:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another aspect of the present invention, cell capture technologies may be used in conjunction with, for example, real-time PCR to provide a more sensitive

tool for detection of metastatic cells expressing lung tumor antigens. Detection of lung cancer cells in biological samples, e.g., bone marrow samples, peripheral blood, and small needle aspiration samples is desirable for diagnosis and prognosis in lung cancer patients.

5 Immunomagnetic beads coated with specific monoclonal antibodies to surface cell markers, or tetrameric antibody complexes, may be used to first enrich or positively select cancer cells in a sample. Various commercially available kits may be used, including Dynabeads® Epithelial Enrich (DynaL Biotech, Oslo, Norway), StemSep™ (StemCell Technologies, Inc., Vancouver, BC), and RosetteSep (StemCell
10 Technologies). A skilled artisan will recognize that other methodologies and kits may also be used to enrich or positively select desired cell populations. Dynabeads® Epithelial Enrich contains magnetic beads coated with mAbs specific for two glycoprotein membrane antigens expressed on normal and neoplastic epithelial tissues. The coated beads may be added to a sample and the sample then applied to a magnet,
15 thereby capturing the cells bound to the beads. The unwanted cells are washed away and the magnetically isolated cells eluted from the beads and used in further analyses.

RosetteSep can be used to enrich cells directly from a blood sample and consists of a cocktail of tetrameric antibodies that targets a variety of unwanted cells and crosslinks them to glycophorin A on red blood cells (RBC) present in the sample,
20 forming rosettes. When centrifuged over Ficoll, targeted cells pellet along with the free RBC. The combination of antibodies in the depletion cocktail determines which cells will be removed and consequently which cells will be recovered. Antibodies that are available include, but are not limited to: CD2, CD3, CD4, CD5, CD8, CD10, CD11b, CD14, CD15, CD16, CD19, CD20, CD24, CD25, CD29, CD33, CD34, CD36, CD38,
25 CD41, CD45, CD45RA, CD45RO, CD56, CD66B, CD66e, HLA-DR, IgE, and TCRαβ.

Additionally, it is contemplated in the present invention that mAbs specific for lung tumor antigens can be generated and used in a similar manner. For example, mAbs that bind to tumor-specific cell surface antigens may be conjugated to magnetic beads, or formulated in a tetrameric antibody complex, and used to enrich or
30 positively select metastatic lung tumor cells from a sample. Once a sample is enriched or positively selected, cells may be lysed and RNA isolated. RNA may then be

subjected to RT-PCR analysis using lung tumor-specific primers in a real-time PCR assay as described herein. One skilled in the art will recognize that enriched or selected populations of cells may be analyzed by other methods (*e.g. in situ* hybridization or flow cytometry).

- 5 In another embodiment, the compositions described herein may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide(s) evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter
10 performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

- Certain *in vivo* diagnostic assays may be performed directly on a tumor.
15 One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

- As noted above, to improve sensitivity, multiple tumor protein markers
20 may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of tumor protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for tumor proteins provided
25 herein may be combined with assays for other known tumor antigens.

- The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a
30 monoclonal antibody or fragment thereof that specifically binds to a tumor protein. Such antibodies or fragments may be provided attached to a support material, as

described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

- 5 Alternatively, a kit may be designed to detect the level of mRNA encoding a tumor protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a tumor protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be
10 present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a tumor protein.

The following examples are offered by way of illustration and not by way of limitation.

EXAMPLES

15 EXAMPLE 1

ISOLATION AND CHARACTERIZATION OF cDNA SEQUENCES ENCODING LUNG TUMOR POLYPEPTIDES

This example illustrates the isolation of cDNA molecules encoding lung tumor-specific polypeptides from lung tumor cDNA libraries.

20 A. ISOLATION OF CDNA SEQUENCES FROM A LUNG SQUAMOUS CELL CARCINOMA LIBRARY

- A human lung squamous cell carcinoma cDNA expression library was constructed from poly A⁺ RNA from a pool of two patient tissues using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies,
25 Gaithersburg, MD) following the manufacturer's protocol. Specifically, lung carcinoma tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A⁺ RNA was then purified using an oligo dT cellulose column as described in

Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with BstXI/EcoRI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with cDNA size fractionation columns (BRL Life Technologies), the cDNA was ligated into the BstXI/NotI site of pcDNA3.1 (Invitrogen) and transformed into ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human lung cDNA expression library was prepared from a pool of four tissue specimens. The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The lung squamous cell carcinoma library contained 2.7×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 2100 base pairs. The normal lung cDNA library contained 1.4×10^6 independent colonies, with 90% of clones having inserts and the average insert size being 1800 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA

cDNA library subtraction was performed using the above lung squamous cell carcinoma and normal lung cDNA libraries, as described by Hara *et al.* (*Blood*, 84:189-199, 1994) with some modifications. Specifically, a lung squamous cell carcinoma-specific subtracted cDNA library was generated as follows. Normal tissue cDNA library (80 μ g) was digested with BamHI and XhoI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 133 μ l of H₂O, heat-denatured and mixed with 133 μ l (133 μ g) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (67 μ l) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μ l H₂O to form the driver DNA.

To form the tracer DNA, 10 μ g lung squamous cell carcinoma cDNA library was digested with NotI and SpeI, phenol chloroform extracted and passed

through Chroma spin-400 columns (Clontech, Palo Alto, CA). Typically, 5 µg of cDNA was recovered after the sizing column. Following ethanol precipitation, the tracer DNA was dissolved in 5 µl H₂O. Tracer DNA was mixed with 15 µl driver DNA and 20 µl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 µl H₂O, mixed with 8 µl driver DNA and 20 µl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA was ligated into NotI/SpeI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a lung squamous cell carcinoma specific subtracted cDNA library (herein after referred to as "lung subtraction I").

A second lung squamous cell carcinoma specific subtracted cDNA library (referred to as "lung subtraction II") was generated in a similar way to the lung subtraction library I, except that eight frequently recovered genes from lung subtraction I were included in the driver DNA, and 24,000 independent clones were recovered.

To analyze the subtracted cDNA libraries, plasmid DNA was prepared from 320 independent clones, randomly picked from the subtracted lung squamous cell carcinoma specific libraries. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A and/or Model 377 (Foster City, CA). The cDNA sequences for sixty isolated clones are provided in SEQ ID NO: 1-60. These sequences were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). No significant homologies were found to the sequences provided in SEQ ID NO: 2, 3, 19, 38 and 46. The sequences of SEQ ID NO: 1, 6-8, 10-13, 15, 17, 18, 20-27, 29, 30, 32, 34-37, 39-45, 47-49, 51, 52, 54, 55 and 57-59 were found to show some homology to previously identified expressed sequence tags (ESTs).

The sequences of SEQ ID NO: 9, 28, 31 and 33 were found to show some homology to previously identified non-human gene sequences and the sequences of SEQ ID NO: 4, 5, 14, 50, 53, 56 and 60 were found to show some homology to gene sequences previously identified in humans.

- 5 The subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer DNA, and the above normal lung tissue cDNA library and a cDNA library from normal liver and heart (constructed from a pool of one sample of each tissue as described above), plus twenty other cDNA clones that were frequently recovered in lung subtractions I and II, as the driver DNA
- 10 (lung subtraction III). The normal liver and heart cDNA library contained 1.76×10^6 independent colonies, with 100% of clones having inserts and the average insert size being 1600 base pairs. Ten additional clones were isolated (SEQ ID NO: 61-70). Comparison of these cDNA sequences with those in the gene bank as described above, revealed no significant homologies to the sequences provided in SEQ ID NO: 62 and
- 15 67. The sequences of SEQ ID NO: 61, 63-66, 68 and 69 were found to show some homology to previously isolated ESTs and the sequence provided in SEQ ID NO: 70 was found to show some homology to a previously identified rat gene.

- In further studies, the subtraction procedure described above was repeated using the above lung squamous cell carcinoma cDNA library as the tracer
- 20 DNA, and a cDNA library from a pool of normal lung, kidney, colon, pancreas, brain, resting PBMC, heart, skin and esophagus as the driver DNA, with esophagus cDNAs making up one third of the driver material. Since esophagus is enriched in normal epithelial cells, including differentiated squamous cells, this procedure is likely to enrich genes that are tumor specific rather than tissues specific. The cDNA sequences
- 25 of 48 clones determined in this subtraction are provided in SEQ ID NO: 177-224. The sequences of SEQ ID NO: 177, 178, 180, 181, 183, 187, 192, 195-197, 208, 211, 212, 215, 216, 218 and 219 showed some homology to previously identified genes. The sequences of SEQ ID NO: 179, 182, 184-186, 188-191, 193, 194, 198-207, 209 210, 213, 214, 217, 220 and 224 showed some homology to previously determined ESTs.
- 30 The sequence of SEQ ID NO: 221-223 showed no homology to any previously determined sequence.

B. ISOLATION OF cDNA SEQUENCES FROM A LUNG
ADENOCARCINOMA LIBRARY

A human lung adenocarcinoma cDNA expression library was constructed as described above. The library contained 3.2×10^6 independent colonies, with 100% of clones having an insert and the average insert size being 1500 base pairs. Library subtraction was performed as described above using the normal lung and normal liver and heart cDNA expression libraries described above as the driver DNA. Twenty-six hundred independent clones were recovered.

Initial cDNA sequence analysis from 100 independent clones revealed many ribosomal protein genes. The cDNA sequences for fifteen clones isolated in this subtraction are provided in SEQ ID NO: 71-86. Comparison of these sequences with those in the gene bank as described above revealed no significant homologies to the sequence provided in SEQ ID NO: 84. The sequences of SEQ ID NO: 71, 73, 74, 77, 78 and 80-82 were found to show some homology to previously isolated ESTs, and the sequences of SEQ ID NO: 72, 75, 76, 79, 83 and 85 were found to show some homology to previously identified human genes.

In further studies, a cDNA library (referred to as mets3616A) was constructed from a metastatic lung adenocarcinoma. The determined cDNA sequences of 25 clones sequenced at random from this library are provided in SEQ ID NO: 255-279. The mets3616A cDNA library was subtracted against a cDNA library prepared from a pool of normal lung, liver, pancreas, skin, kidney, brain and resting PBMC. To increase the specificity of the subtraction, the driver was spiked with genes that were determined to be most abundant in the mets3616A cDNA library, such as EF1-alpha, integrin-beta and anticoagulant protein PP4, as well as with cDNAs that were previously found to be differentially expressed in subtracted lung adenocarcinoma cDNA libraries. The determined cDNA sequences of 51 clones isolated from the subtracted library (referred to as mets3616A-S1) are provided in SEQ ID NO: 280-330.

Comparison of the sequences of SEQ ID NO: 255-330 with those in the public databases revealed no significant homologies to the sequences of SEQ ID NO: 255-258, 260, 262-264, 270, 272, 275, 276, 279, 281, 287, 291, 296, 300 and 310. The sequences of SEQ ID NO: 259, 261, 265-269, 271, 273, 274, 277, 278, 282-285, 288-

290, 292, 294, 297-299, 301, 303-309, 313, 314, 316, 320-324 and 326-330 showed some homology to previously identified gene sequences, while the sequences of SEQ ID NO: 280, 286, 293, 302, 310, 312, 315, 317-319 and 325 showed some homology to previously isolated expressed sequence tags (ESTs).

5

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF LUNG TUMOR POLYPEPTIDES

Using gene specific primers, mRNA expression levels for seven representative lung tumor polypeptides described in Example 1 were examined in a variety of normal and tumor tissues using RT-PCR.

10

Briefly, total RNA was extracted from a variety of normal and tumor tissues using Trizol reagent as described above. First strand synthesis was carried out using 2 μ g of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β -actin was used as an internal control for each of the tissues examined. 1 μ l of 1:30 dilution of cDNA was employed to enable the linear range amplification of the β -actin template and was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β -actin levels were determined for each reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

15

20

25

mRNA Expression levels were examined in five different types of tumor tissue (lung squamous cell carcinoma from 3 patients, lung adenocarcinoma, colon tumor from 2 patients, breast tumor and prostate tumor), and thirteen different normal tissues (lung from 4 donors, prostate, brain, kidney, liver, ovary, skeletal muscle, skin, small intestine, stomach, myocardium, retina and testes). Using a 10-fold amount of cDNA, the antigen LST-S1-90 (SEQ ID NO: 3) was found to be expressed at high levels in lung squamous cell carcinoma and in breast tumor, and at low to undetectable levels in the other tissues examined.

The antigen LST-S2-68 (SEQ ID NO: 15) appears to be specific to lung and breast tumor, however, expression was also detected in normal kidney. Antigens LST-S1-169 (SEQ ID NO: 6) and LST-S1-133 (SEQ ID NO: 5) appear to be very abundant in lung tissues (both normal and tumor), with the expression of these two genes being decreased in most of the normal tissues tested. Both LST-S1-169 and LST-S1-133 were also expressed in breast and colon tumors. Antigens LST-S1-6 (SEQ ID NO: 7) and LST-S2-I2-5F (SEQ ID NO: 47) did not show tumor or tissue specific expression, with the expression of LST-S1-28 being rare and only detectable in a few tissues. The antigen LST-S3-7 (SEQ ID NO: 63) showed lung and breast tumor specific expression, with its message only being detected in normal testes when the PCR was performed for 30 cycles. Lower level expression was detected in some normal tissues when the cycle number was increased to 35. Antigen LST-S3-13 (SEQ ID NO: 66) was found to be expressed in 3 out of 4 lung tumors, one breast tumor and both colon tumor samples. Its expression in normal tissues was lower compared to tumors, and was only detected in 1 out of 4 normal lung tissues and in normal tissues from kidney, ovary and retina. Expression of antigens LST-S3-4 (SEQ ID NO: 62) and LST-S3-14 (SEQ ID NO: 67) was rare and did not show any tissue or tumor specificity. Consistent with Northern blot analyses, the RT-PCR results on antigen LAT-S1-A-10A (SEQ ID NO: 78) suggested that its expression is high in lung, colon, stomach and small intestine tissues, including lung and colon tumors, whereas its expression was low or undetectable in other tissues.

A total of 2002 cDNA fragments isolated in lung subtractions I, II and III, described above, were colony PCR amplified and their mRNA expression levels in lung tumor, normal lung, and various other normal and tumor tissues were determined using microarray technology (Synteni, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity. Seventeen non-redundant cDNA clones showed over-expression in lung

squamous tumors, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or 10-fold less compared to lung squamous tumors. The determined cDNA sequences for the clone L513S are provided in SEQ ID NO: 87 and 88; those for L514S are provided in SEQ ID NO: 89 and 90; those for L516S in SEQ ID NO: 91 and 92; that for L517S in SEQ ID NO: 93; that for L519S in SEQ ID NO: 94; those for L520S in SEQ ID NO: 95 and 96; those for L521S in SEQ ID NO: 97 and 98; that for L522S in SEQ ID NO: 99; that for L523S in SEQ ID NO: 100; that for L524S in SEQ ID NO: 101; that for L525S in SEQ ID NO: 102; that for L526S in SEQ ID NO: 103; that for L527S in SEQ ID NO: 104; that for L528S in SEQ ID NO: 105; that for L529S in SEQ ID NO: 106; and those for L530S in SEQ ID NO: 107 and 108. Additionally, the full-length cDNA sequence for L530S is provided in SEQ ID NO: 151, with the corresponding amino acid sequence being provided in SEQ ID NO: 152. L530S shows homology to a splice variant of a p53 tumor suppressor homologue, p63. The cDNA sequences of 7 known isoforms of p63 are provided in SEQ ID NO: 331-337, with the corresponding amino acid sequences being provided in SEQ ID NO: 338-344, respectively.

Due to polymorphisms, the clone L531S appears to have two forms. A first determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 109, with the corresponding amino acid sequence being provided in SEQ ID NO: 110. A second determined full-length cDNA sequence for L531S is provided in SEQ ID NO: 111, with the corresponding amino acid sequence being provided in SEQ ID NO: 112. The sequence of SEQ ID NO: 111 is identical to that of SEQ ID NO: 109, except that it contains a 27 bp insertion. Similarly, L514S has two alternatively spliced forms; the first variant cDNA is listed as SEQ ID NO: 153, with the corresponding amino acid sequence being provided in SEQ ID NO: 155. The full-length cDNA for the second variant form of L514S is provided in SEQ ID NO: 154, with the corresponding amino acid sequence being provided in SEQ ID NO: 156.

Full length cloning for L524S (SEQ ID NO: 101) yielded two variants (SEQ ID NO: 163 and 164) with the corresponding amino acid sequences of SEQ ID

NO: 165 and 166, respectively. Both variants have been shown to encode parathyroid hormone-related peptide.

Attempts to isolate the full-length cDNA for L519S, resulted in the isolation of the extended cDNA sequence provided in SEQ ID NO: 173, which contains
5 a potential open reading frame. The amino acid sequence encoded by the sequence of SEQ ID NO: 173 is provided in SEQ ID NO: 174. Additionally, the full-length cDNA sequence for the clone of SEQ ID NO: 100 (known as L523S), a known gene, is provided in SEQ ID NO: 175, with the corresponding amino acid sequence being provided in SEQ ID NO: 176. In further studies, a full-length cDNA sequence for
10 L523S was isolated from a L523S-positive tumor cDNA library by PCR amplification using gene specific primers designed from the sequence of SEQ ID NO: 175. The determined full-length cDNA sequence is provided in SEQ ID NO: 347. The amino acid sequence encoded by this sequence is provided in SEQ ID NO: 348. This protein sequence differs from the previously published protein sequence at two amino acid
15 positions, namely at positions 158 and 410.

Comparison of the sequences of L514S and L531S (SEQ ID NO: 87 and 88, and 109, respectively) with those in the gene bank, as described above, revealed no significant homologies to known sequences. The sequences of L513S, L516S, L517S, L519S, L520S and L530S (SEQ ID NO: 87 and 88, 91 and 92, 93, 94, 95 and 96, 107
20 and 108, respectively) were found to show some homology to previously identified ESTs. The sequences of L521S, L522S, L523S, L524S, L525S, L526S, L527S, L528S and L529S (SEQ ID NO: 97 and 98, 99, 99, 101, 102, 103, 104, 105, and 106, respectively) were found to represent known genes. The determined full-length cDNA sequence for L520S is provided in SEQ ID NO: 113, with the corresponding amino
25 acid sequence being provided in SEQ ID NO: 114. Subsequent microarray analysis showed L520S to be overexpressed in breast tumors in addition to lung squamous tumors.

Further analysis demonstrated that L529S (SEQ ID NO: 106 and 115), L525S (SEQ ID NO: 102 and 120) and L527S (SEQ ID NO: 104) are cytoskeletal
30 components and potentially squamous cell specific proteins. L529S is connexin 26, a gap junction protein. It was found to be highly expressed in one lung squamous tumor,

referred to as 9688T, and moderately over-expressed in two others. However, lower level expression of connexin 26 is also detectable in normal skin, colon, liver and stomach. The over-expression of connexin 26 in some breast tumors has been reported and a mutated form of L529S may result in over-expression in lung tumors. L525S is
5 plakophilin 1, a desmosomal protein found in plaque-bearing adhering junctions of the skin. Expression levels for L525S mRNA was highly elevated in three out of four lung squamous tumors tested, and in normal skin. L527S has been identified as keratin 6 isoform, type II 58 Kd keratin and cytokeratin 13, and shows over-expression in squamous tumors and low expression in normal skin, breast and colon tissues. Keratin
10 and keratin-related genes have been extensively documented as potential markers for lung cancer including CYFRA2.1 (Pastor, A., et al, *Eur. Respir. J.*, 10:603-609, 1997). L513S (SEQ ID NO: 87 and 88) shows moderate over-expression in several tumor tissues tested, and encodes a protein that was first isolated as a pemphigus vulgaris antigen.

15 L520S (SEQ ID NO: 95 and 96) and L521S (SEQ ID NO: 97 and 98) are highly expressed in lung squamous tumors, with L520S being up-regulated in normal salivary gland and L521S being over-expressed in normal skin. Both belong to a family of small proline rich proteins and represent markers for fully differentiated squamous cells. L521S has been described as a specific marker for lung squamous tumor (Hu, R.,
20 et al, *Lung Cancer*, 20:25-30, 1998). L515S (SEQ ID NO: 162) encodes IGF-β2 and L516S is an aldose reductase homologue. Both are moderately expressed in lung squamous tumors and in normal colon. Notably, L516S (SEQ ID NO: 91 and 92) is up-regulated in metastatic tumors but not primary lung adenocarcinoma, an indication of its potential role in metatasis and a potential prognostic marker. L522S (SEQ ID NO: 99)
25 is moderately over-expressed in lung squamous tumors with minimum expression in normal tissues. L522S has been shown to belong to a class IV alcohol dehydrogenase, ADH7, and its expression profile suggests it is a squamous cell specific antigen. L523S (SEQ ID NO: 100) is moderately over-expressed in lung squamous tumor, human pancreatic cancer cell lines and pancreatic cancer tissues, suggesting this gene may be a
30 shared antigen between pancreatic and lung squamous cell cancer.

L524S (SEQ ID NO: 101) is over-expressed in the majority of squamous tumors tested and is homologous with parathyroid hormone-related peptide (PTHrP), which is best known to cause humoral hypercalcaemia associated with malignant tumors such as leukemia, prostate and breast cancer. It is also believed that PTHrP is most commonly associated with squamous carcinoma of lung and rarely with lung adenocarcinoma (Davidson, L.A., et al, *J. Pathol.*, 178: 398-401, 1996). L528S (SEQ ID NO: 105) is highly over-expressed in two lung squamous tumors with moderate expression in two other squamous tumors, one lung adenocarcinoma and some normal tissues, including skin, lymph nodes, heart, stomach and lung. It encodes the NMB gene that is similar to the precursor of melanocyte specific gene Pmel17, which is reported to be preferentially expressed in low-metastatic potential melanoma cell lines. This suggests that L528S may be a shared antigen in both melanoma and lung squamous cell carcinoma. L526S (SEQ ID NO: 103) was overexpressed in all lung squamous cell tumor tissues tested and has been shown to share homology with a gene (ATM) in which a mutation causes ataxia telangiectasia, a genetic disorder in humans causing a predisposition to cancer, among other symptoms. ATM encodes a protein that activates a p53 mediated cell-cycle checkpoint through direct binding and phosphorylation of the p53 molecule. Approximately 40% of lung cancers are associated with p53 mutations, and it is speculated that over-expression of ATM is a result of compensation for loss of p53 function, but it is unknown whether over-expression is the cause of result of lung squamous cell carcinoma. Additionally, expression of L526S (ATM) is also detected in a metastatic but not lung adenocarcinoma, suggesting a role in metastasis.

Expression of L523S (SEQ ID NO: 175), was examined by real time RT-PCR as described above. In a first study using a panel of lung squamous tumors, L523S was found to be expressed in 4/7 lung squamous tumors, 2/3 head and neck squamous tumors and 2/2 lung adenocarcinomas, with low level expression being observed in skeletal muscle, soft palate and tonsil. In a second study using a lung adenocarcinoma panel, expression of L523S was observed in 4/9 primary adenocarcinomas, 2/2 lung pleural effusions, 1/1 metastatic lung adenocarcinomas and 2/2 lung squamous tumors, with little expression being observed in normal tissues.

Expression of L523S in lung tumors and various normal tissues was also examined by Northern blot analysis, using standard techniques. In a first study, L523S was found to be expressed in a number of lung adenocarcinomas and squamous cell carcinomas, as well as normal tonsil. No expression was observed in normal lung. In a second study using a normal tissue blot (referred to as HB-12) from Clontech, no expression was observed in brain, skeletal muscle, colon, thymus, spleen, kidney, liver, small intestine, lung or PBMC, although there was strong expression in placenta.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES BY PCR-BASED SUBTRACTION

10

Eight hundred and fifty seven clones from a cDNA subtraction library, containing cDNA from a pool of two human lung squamous tumors subtracted against eight normal human tissue cDNAs including lung, PBMC, brain, heart, kidney, liver, pancreas, and skin, (Clontech, Palo Alto, CA) were derived and submitted to a first round of PCR amplification. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the P7-Adv vector (Clontech, Palo Alto, CA) and transformed into DH5 α *E. coli* (Gibco, BRL). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

20

One hundred and sixty two positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the EMBL and GenBank databases, as described above, revealed no significant homologies to 13 of these clones, hereinafter referred to as Contigs 13, 16, 17, 19, 22, 24, 29, 47, 49, 56-59. The determined cDNA sequences for these clones are provided in SEQ ID NO: 125, 127-129, 131-133, 142, 144, 148-150, and 157, respectively. Contigs 1, 3-5, 7-10, 12, 11, 15, 20, 31, 33, 38, 39, 41, 43, 44, 45, 48, 50, 53, 54 (SEQ ID NO: 115-124, 126, 130, 134-141, 143, 145-147, respectively) were found to show some degree of homology to previously identified DNA sequences. Contig 57 (SEQ ID NO: 149) was found to represent the clone L519S

25

(SEQ ID NO: 94) disclosed in US. Patent Application No. 09/123,912, filed July 27, 1998. To the best of the inventors' knowledge, none of these sequences have been previously shown to be differentially over-expressed in lung tumors.

mRNA expression levels for representative clones in lung tumor tissues,
5 normal lung tissues (n=4), resting PBMC, salivary gland, heart, stomach, lymph nodes, skeletal muscle, soft palate, small intestine, large intestine, bronchial, bladder, tonsil, kidney, esophagus, bone marrow, colon, adrenal gland, pancreas, and skin (all derived from human) were determined by RT-PCR as described above. Expression levels using microarray technology, as described above, were examined in one sample of each tissue
10 type unless otherwise indicated.

Contig 3 (SEQ ID NO: 116) was found to be highly expressed in all head and neck squamous cell tumors tested (17/17), and expressed in the majority (8/12) of lung squamous tumors, (high expression in 7/12, moderate in 2/12, and low in 2/12), while showing negative expression for 2/4 normal lung tissues and low expression in
15 the remaining two samples. Contig 3 showed moderate expression in skin and soft palate, and lowered expression levels in resting PBMC, large intestine, salivary gland, tonsil, pancreas, esophagus, and colon. Contig 11 (SEQ ID NO: 124) was found to be expressed in all head and neck squamous cell tumors tested (17/17), with high levels of expression being seen in 14/17 tumors, and moderately levels of expression being seen
20 in 3/17 tumors. Additionally, high expression was seen in 3/12 lung squamous tumors and moderate expression in 4/12 lung squamous tumors. Contig 11 was negative for 3/4 normal lung samples, with the remaining sample having only low expression. Contig 11 showed low to moderate reactivity to salivary gland, soft palate, bladder, tonsil, skin, esophagus, and large intestine. Contig 13 (SEQ ID NO: 125) was found to be expressed
25 in all head and neck squamous cell tumors tested (17/17), with high expression in 12/17, and moderate expression in 5/17. Contig 13 was expressed in 7/12 lung squamous tumors, with high expression in 4/12 and moderate expression in three samples. Analysis of normal lung samples showed negative expression for 2/4 and low to moderate expression in the remaining two samples. Contig 13 showed low to
30 moderate reactivity to resting PBMC, salivary gland, bladder, pancreas, tonsil, skin, esophagus, and large intestine, as well as high expression in soft palate. Subsequent

full-length cloning efforts revealed that contig 13 (also known as L761P) maps to the 3' untranslated region of the hSec10p gene. The full-length sequence for this gene is set forth in SEQ ID NO: 368, and encodes the protein set forth in SEQ ID NO: 369.

Contig 16 (SEQ ID NO: 127) was found to be moderately expressed in
5 several head and neck squamous cell tumors (6/17) and one lung squamous tumor, while showing no expression in any normal lung samples tested. Contig 16 showed low reactivity to resting PBMC, large intestine, skin, salivary gland, and soft palate. Contig 17 (SEQ ID NO: 128) was shown to be expressed in all head and neck squamous cell tumors tested (17/17) (highly expressed in 5/17, and moderately expressed in 12/17).
10 Determination of expression levels in lung squamous tumors showed one tumor sample with high expression and 3/12 with moderate levels. Contig 17 was negative for 2/4 normal lung samples, with the remaining samples having only low expression. Additionally, low level expression was found in esophagus and soft palate. Contig 19 (SEQ ID NO: 129) was found to be expressed in most head and neck squamous cell
15 tumors tested (11/17); with two samples having high expression levels, 6/17 showing moderate expression, and low expression being found in 3/17. Testing in lung squamous tumors revealed only moderate expression in 3/12 samples. Expression levels in 2/4 of normal lung samples were negative, the two other samples having only low expression. Contig 19 showed low expression levels in esophagus, resting PBMC,
20 salivary gland, bladder, soft palate and pancreas.

Contig 22 (SEQ ID NO: 131), was shown to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in four of these samples, moderate expression in 6/17, and low expression in 3/17. Expression levels in lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with
25 negative expression in two normal lung samples and low expression in two other samples (n=4). Contig 22 showed low expression in skin, salivary gland and soft palate. Similarly, Contig 24 (SEQ ID NO: 132) was found to be expressed in most head and neck squamous cell tumors tested (13/17) with high expression in three of these samples, moderate expression in 6/17, and low expression in 4/17. Expression levels in
30 lung squamous tumors were found to be moderate to high for 3/12 tissues tested, with negative expression for three normal lung samples and low expression in one sample

(n=4). Contig 24 showed low expression in skin, salivary gland and soft palate. Contig 29 (SEQ ID NO: 133) was expressed in nearly all head and neck squamous cell tumors tested (16/17): highly expressed in 4/17, moderately expressed in 11/17, with low expression in one sample. Also, it was moderately expressed in 3/12 lung squamous tumors, while being negative for 2/4 normal lung samples. Contig 29 showed low to moderate expression in large intestine, skin, salivary gland, pancreas, tonsil, heart and soft palate. Contig 47 (SEQ ID NO: 142) was expressed in most head and neck squamous cell tumors tested (12/17): moderate expression in 10/17, and low expression in two samples. In lung squamous tumors, it was highly expressed in one sample and moderately expressed in two others (n=13). Contig 47 was negative for 2/4 normal lung samples, with the remaining two samples having moderate expression. Also, Contig 47 showed moderate expression in large intestine, and pancreas, and low expression in skin, salivary gland, soft palate, stomach, bladder, resting PBMC, and tonsil.

Contig 48 (SEQ ID NO: 143) was expressed in all head and neck squamous cell tumors tested (17/17): highly expressed in 8/17 and moderately expressed in 7/17, with low expression in two samples. Expression levels in lung squamous tumors were high to moderate in three samples (n=13). Contig 48 was negative for one out of four normal lung samples, the remaining showing low or moderate expression. Contig 48 showed moderate expression in soft palate, large intestine, pancreas, and bladder, and low expression in esophagus, salivary gland, resting PBMC, and heart. Contig 49 (SEQ ID NO: 144) was expressed at low to moderate levels in 6/17 head and neck squamous cell tumors tested. Expression levels in lung squamous tumors were moderate in three samples (n=13). Contig 49 was negative for 2/4 normal lung samples, the remaining samples showing low expression. Moderate expression levels in skin, salivary gland, large intestine, pancreas, bladder and resting PBMC were shown, as well as low expression in soft palate, lymph nodes, and tonsil. Contig 56 (SEQ ID NO: 148) was expressed in low to moderate levels in 3/17 head and neck squamous cell tumors tested, and in lung squamous tumors, showing low to moderate levels in three out of thirteen samples. Notably, low expression levels were detected in one adenocarcinoma lung tumor sample (n=2). Contig 56 was negative for

3/4 normal lung samples, and showed moderate expression levels in only large intestine, and low expression in salivary gland, soft palate, pancreas, bladder, and resting PBMC. Contig 58, also known as L769P, (SEQ ID NO: 150) was expressed at moderate levels in 11/17 head and neck squamous cell tumors tested and low expression in one additional sample. Expression in lung squamous tumors showed low to moderate levels in three out of thirteen samples. Contig 58 was negative for 3/4 normal lung samples, with one sample having low expression. Moderate expression levels in skin, large intestine, and resting PBMC were demonstrated, as well as low expression in salivary gland, soft palate, pancreas, and bladder. Contig 59 (SEQ ID NO: 157) was expressed in some head, neck, and lung squamous tumors. Low level expression of Contig 59 was also detected in salivary gland and large intestine.

The full-length cDNA sequence for Contig 22, also referred to as L763P, is provided in SEQ ID NO: 158, with the corresponding amino acid sequence being provided in SEQ ID NO: 159. Real-time RT-PCR analysis of L763P revealed that it is highly expressed in 3/4 lung squamous tumors as well as 4/4 head and neck squamous tumors, with low level expression being observed in normal brain, skin, soft pallet and trachea. Subsequent database searches revealed that the sequence of SEQ ID NO: 158 contains a mutation, resulting in a frameshift in the corresponding protein sequence. A second cDNA sequence for L763P is provided in SEQ ID NO: 345, with the corresponding amino acid sequence being provided in SEQ ID NO: 346. The sequences of SEQ ID NO: 159 and 346 are identical with the exception of the C-terminal 33 amino acids of SEQ ID NO: 159.

The full-length cDNA sequence incorporating Contigs 17, 19, and 24, referred to as L762P, is provided in SEQ ID NO: 160, with the corresponding amino acid sequence being provided in SEQ ID NO: 161. Further analysis of L762P has determined it to be a type I membrane protein and two additional variants have been sequenced. Variant 1 (SEQ ID NO: 167, with the corresponding amino acid sequence in SEQ ID NO: 169) is an alternatively spliced form of SEQ ID NO: 160 resulting in deletion of 503 nucleotides, as well as deletion of a short segment of the expressed protein. Variant 2 (SEQ ID NO: 168, with the corresponding amino acid sequence in SEQ ID NO: 170) has a two nucleotide deletion at the 3' coding region in comparison

to SEQ ID NO: 160, resulting in a secreted form of the expressed protein. Real-time RT-PCR analysis of L762P revealed that is over-expressed in 3/4 lung squamous tumors and 4/4 head & neck tumors, with low level expression being observed in normal skin, soft pallet and trachea.

- 5 An epitope of L762P was identified as having the sequence KPGHWTYTLNNTTHSLQALK (SEQ ID NO: 382), which corresponds to amino acids 571-590 of SEQ ID NO:161.

- The full-length cDNA sequence for contig 56 (SEQ ID NO: 148), also referred to as L773P, is provided in SEQ ID NO: 171, with the amino acid sequence in
10 SEQ ID NO: 172. L773P was found to be identical to dihydroxyl dehydrogenase at the 3' portion of the gene, with divergent 5' sequence. As a result, the 69 N-terminal amino acids are unique. The cDNA sequence encoding the 69 N-terminal amino acids is provided in SEQ ID NO: 349, with the N-terminal amino acid sequence being provided in SEQ ID NO: 350. Real-time PCR revealed that L773P is highly expressed in lung
15 squamous tumor and lung adenocarcinoma, with no detectable expression in normal tissues. Subsequent Northern blot analysis of L773P demonstrated that this transcript is differentially over-expressed in squamous tumors and detected at approximately 1.6 Kb in primary lung tumor tissue and approximately 1.3 Kb in primary head and neck tumor tissue.

- 20 Subsequent microarray analysis has shown Contig 58, also referred to as L769S (SEQ ID NO: 150), to be overexpressed in breast tumors in addition to lung squamous tumors.

EXAMPLE 4

ISOLATION AND CHARACTERIZATION OF LUNG TUMOR POLYPEPTIDES

- 25 BY PCR-BASED SUBTRACTION

Seven hundred and sixty clones from a cDNA subtraction library, containing cDNA from a pool of two human lung primary adenocarcinomas subtracted against a pool of nine normal human tissue cDNAs including skin, colon, lung, esophagus, brain, kidney, spleen, pancreas and liver, (Clontech, Palo Alto, CA) were

derived and submitted to a first round of PCR amplification. This library (referred to as ALT-1) was subjected to a second round of PCR amplification, following the manufacturer's protocol. The expression levels of these 760 cDNA clones in lung tumor, normal lung, and various other normal and tumor tissues, were examined using microarray technology (Incyte, Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence intensity was measured. This intensity correlates with the hybridization intensity.. A total of 118 clones, of which 55 were unique, were found to be over-expressed in lung tumor tissue, with expression in normal tissues tested (lung, skin, lymph node, colon, liver, pancreas, breast, heart, bone marrow, large intestine, kidney, stomach, brain, small intestine, bladder and salivary gland) being either undetectable, or at significantly lower levels. One of these clones, having the sequence as provided in SEQ ID NO:420 (clone #19014), shows homology to a previously identified clone, L773P. Clone L773P has the full-length cDNA sequence provided in SEQ ID NO:171 and the amino acid sequence provided in SEQ ID NO:172 The isolation of clone #19014 is also described in co-pending U.S. Patent application 09/285,479, filed April 2, 1999.

20

EXAMPLE 5

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support is carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides are precipitated in cold methyl-t-

butyl-ether. The peptide pellets are then dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure
5 fractions, the peptides are characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

EXAMPLE 6

PREPARATION OF ANTIBODIES AGAINST LUNG CANCER ANTIGENS

Polyclonal antibodies against the lung cancer antigens L514S, L528S,
10 L531S, L523 and L773P (SEQ ID NO: 155, 225, 112, 176 and 171, respectively) were prepared as follows.

Rabbits were immunized with recombinant protein expressed in and purified from *E. coli* as described below. For the initial immunization, 400 µg of antigen combined with muramyl dipeptide (MDP) was injected subcutaneously (S.C.).
15 Animals were boosted S.C. 4 weeks later with 200 µg of antigen mixed with incomplete Freund's Adjuvant (IFA). Subsequent boosts of 100 µg of antigen mixed with IFA were injected S.C. as necessary to induce high antibody titer responses. Serum bleeds from immunized rabbits were tested for antigen-specific reactivity using ELISA assays with purified protein. Polyclonal antibodies against L514S, L528S, L531S, L523S and
20 L773P were affinity purified from high titer polyclonal sera using purified protein attached to a solid support.

Immunohistochemical analysis using polyclonal antibodies against L514S was performed on a panel of 5 lung tumor samples, 5 normal lung tissue samples and normal colon, kidney, liver, brain and bone marrow. Specifically, tissue samples
25 were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with antibody for 1 hr. HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize L514S immunoreactivity. L514S was found to be highly expressed in lung tumor tissue with little or no expression being observed in

normal lung, brain or bone marrow. Light staining was observed in colon (epithelial crypt cells positive) and kidney (tubules positive). Staining was seen in normal liver but no mRNA has been detected in this tissue making this result suspect.

Using the same procedure, immunohistochemical analysis using polyclonal antibodies against L528S demonstrated staining in lung tumor and normal lung samples, light staining in colon and kidney, and no staining in liver and heart.

Immunohistochemical analysis using polyclonal antibodies against L531S demonstrated staining in lung tumor samples, light membrane staining in most normal lung samples, epithelial staining in colon, tubule staining in kidney, ductal epithelial staining in liver and no staining in heart.

Immunohistochemical analysis using polyclonal antibodies against L523S demonstrated staining in all lung cancer samples tested but no staining in normal lung, kidney, liver, colon, bone marrow or cerebellum.

Generation of polyclonal anti-sera against L762P (SEQ ID NO: 169 and 170) was performed as follows. 400 micrograms of lung antigen was combined with 100 micrograms of muramyl dipeptide (MDP). An equal volume of Incomplete Freund's Adjuvant (IFA) was added and then mixed until an emulsion was formed. Rabbits were injected subcutaneously (S.C.). After four weeks the animals were injected S.C. with 200 micrograms of antigen mixed with an equal volume of IFA. Every four weeks animals were boosted with 100 micrograms of antigen. Seven days following each boost the animal was bled. Sera was generated by incubating the blood at 4°C for 12-24 hours followed by centrifugation.

Characterization of polyclonal antisera was carried out as follows. Ninety-six well plates were coated with antigen by incubating with 50 microliters (typically 1 microgram) at 4°C for 20 hrs. 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hrs. Plates were washed 6 times with PBS/0.01% Tween. Rabbit sera was diluted in PBS and 50 microliters of diluted sera was added to each well and incubated at room temperature for 30 min. Plates were washed as described above before addition of 50 microliters of goat anti-rabbit horse radish peroxidase (HRP) at a 1:10000 dilution and incubation at room temperature for 30 min. Plates were washed as described above and 100µl of TMB

Microwell Peroxidase Substrate was added to each well. Following a 15 minute incubation in the dark at room temperature, the colorimetric reaction was stopped with 100µl 1N H₂SO₄ and read immediately at 450 nm. Antisera showed strong reactivity to antigen L762P.

- 5 Immunohistochemical analysis using polyclonal antibodies against L762P demonstrated staining in all lung cancer samples tested, some light staining in the bronchiole epithelium of normal lung, tubule staining in kidney, light epithelial staining in colon and no staining in heart or liver.

- 10 In order to evaluate L773P protein expression in various tissues, immunohistochemistry (IHC) analysis was performed using an affinity purified L773P polyclonal antibody. Briefly, tissue samples were fixed in formalin solution for 12-24 hrs and embedded in paraffin before being sliced into 8 micron sections. Steam heat induced epitope retrieval (SHIER) in 0.1 M sodium citrate buffer (pH 6.0) was used for optimal staining conditions. Sections were incubated with 10% serum/PBS for 5
- 15 minutes. Primary antibody was added to each section for 25 minutes at indicated concentrations followed by 25 minute incubation with either anti-rabbit or anti-mouse biotinylated antibody. Endogenous peroxidase activity was blocked by three 1.5 minute incubations with hydrogen peroxidase. The avidin biotin complex/horse radish peroxidase (ABC/HRP) system was used along with DAB chromogen to visualize
- 20 L773P expression. Slides were counterstained with hematoxylin to visualize cell nuclei. Using this approach, L773P protein was detected in 6/8 lung tumors, 4/6 normal lung samples (very light staining in some cases), 1/1 kidney samples (very light staining), 0/1 heart samples, 1/1 colon samples (very light staining) and 0/1 liver samples.

25

EXAMPLE 7

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

Immunogenic peptides from the lung cancer antigen L762P (SEQ ID NO: 161) for HLA-A2/K^b-restricted CD8⁺ T cells were identified as follows.

The location of HLA-A2 binding peptides within the lung cancer antigen L762P (SEQ ID NO: 161) was predicted using a computer program which predicts peptide sequences likely to be to HLA-A*0201 by fitting to the known peptide binding motif for HLA-A*0201 (Rupert *et al.* (1993) *Cell* 74:929; Rammensee *et al.* (1995) *Immunogenetics* 41:178-228). A series of 19 synthetic peptides corresponding to a selected subset of the predicted HLA-A*0201 binding peptides was prepared as described above.

Mice expressing the transgene for human HLA A2/K^b (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with the synthetic peptides, as described by Theobald *et al.*, *Proc. Natl. Acad. Sci. USA* 92:11993-11997, 1995, with the following modifications. Mice were immunized with 50µg of L726P peptide and 120µg of an I-A^b binding peptide derived from hepatitis B virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared. Cells were then resuspended at 7 x 10⁶ cells/ml in complete media (RPMI-1640; Gibco BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2 x 10⁻⁵ M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) L762P peptide- (5µg/ml) and 10mg/ml B₂-microglobulin- (3 µg/ml) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). After six days, cells (5 x 10⁵/ml) were restimulated with 2.5 x 10⁶/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman *et al.*, *Science* 258:815-818, 1992) and 5 x 10⁶/ml irradiated (3000 rads) A2/K^b-transgenic spleen feeder cells. Cells were cultured in the presence of 10U/ml IL-2. Cells were restimulated on a weekly basis as described, in preparation for cloning the line.

Peptide-specific cell lines were cloned by limiting dilution analysis with irradiated (20,000 rads) L762P peptide-pulsed EL4 A2Kb tumor cells (1 x 10⁴ cells/well) as stimulators and irradiated (3000 rads) A2/K^b-transgenic spleen cells as feeders (5 x 10⁵ cells/well) grown in the presence of 10U/ml IL-2. On day 7, cells were restimulated as before. On day 14, clones that were growing were isolated and maintained in culture.

Cell lines specific for the peptides L762P-87 (SEQ ID NO: 226; corresponding to amino acids 87-95 of SEQ ID NO: 161), L762P-145 (SEQ ID NO: 227; corresponding to amino acids 145-153 of SEQ ID NO: 161), L762P-585 (SEQ ID NO: 228; corresponding to amino acids 585-593 of SEQ ID NO: 161), L762P-425 (SEQ ID NO: 229; corresponding to amino acids 425-433 of SEQ ID NO: 161), L762P(10)-424 (SEQ ID NO: 230; corresponding to amino acids 424-433 of SEQ ID NO: 161) and L762P(10)-458 (SEQ ID NO: 231; corresponding to amino acids 458-467 of SEQ ID NO: 161) demonstrated significantly higher reactivity (as measured by percent specific lysis) against L762P peptide-pulsed EL4-A2/K^b tumor target cells than control peptide-pulsed EL4-A2/K^b tumor target cells.

EXAMPLE 8

IDENTIFICATION OF CD4 IMMUNOGENIC T CELL EPITOPES DERIVED FROM THE LUNG CANCER ANTIGEN L762P

CD4 T cell lines specific for the antigen L762P (SEQ ID NO: 161) were generated as follows.

A series of 28 overlapping peptides were synthesized that spanned approximately 50% of the L762P sequence. For priming, peptides were combined into pools of 4-5 peptides, pulsed at 20 micrograms/ml into dendritic cells for 24 hours. The dendritic cells were then washed and mixed with positively selected CD4⁺ T cells in 96 well U-bottomed plates. Forty cultures were generated for each peptide pool. Cultures were restimulated weekly with fresh dendritic cells loaded with peptide pools. Following a total of 3 stimulation cycles, cells were rested for an additional week and tested for specificity to antigen presenting cells (APC) pulsed with peptide pools using interferon-gamma ELISA and proliferation assays. For these assays, adherent monocytes loaded with either the relevant peptide pool or an irrelevant peptide were used as APC. T cell lines that appeared to specifically recognize L762P peptide pools both by cytokine release and proliferation were identified for each pool. Emphasis was placed on identifying T cells with proliferative responses. T cell lines that demonstrated either both L762P-specific cytokine secretion and proliferation, or strong proliferation

alone were further expanded to be tested for recognition of individual peptides from the pools, as well as for recognition of recombinant L762P. The source of recombinant L762P was *E. coli*, and the material was partially purified and endotoxin positive. These studies employed 10 micrograms of individual peptides, 10 or 2 micrograms of an irrelevant peptide, and 2 or 0.5 micrograms of either L762P protein or an irrelevant, equally impure, *E. coli* generated recombinant protein. Significant interferon-gamma production and CD4 T cell proliferation was induced by a number of L762P-derived peptides in each pool. The amino acid sequences for these peptides are provided in SEQ ID NO: 232-251. These peptides correspond to amino acids 661-680, 676-696, 526-545, 874-893, 811-830, 871-891, 856-875, 826-845, 795-815, 736-755, 706-725, 706-725, 691-710, 601-620, 571-590, 556-575, 616-635, 646-665, 631-650, 541-560 and 586-605, respectively, of SEQ ID NO: 161.

CD4 T cell lines that demonstrated specificity for individual L762P-derived peptides were further expanded by stimulation with the relevant peptide at 10 micrograms/ml. Two weeks post-stimulation, T cell lines were tested using both proliferation and IFN-gamma ELISA assays for recognition of the specific peptide. A number of previously identified T cells continued to demonstrate L762P-peptide specific activity. Each of these lines was further expanded on the relevant peptide and, following two weeks of expansion, tested for specific recognition of the L762P-peptide in titration experiments, as well as for recognition of recombinant *E. coli*-derived L762P protein. For these experiments, autologous adherent monocytes were pulsed with either the relevant L762P-derived peptide, an irrelevant mammaglobin-derived peptide, recombinant *E. coli*-derived L762P (approx. 50% pure), or an irrelevant *E. coli*-derived protein. The majority of T cell lines were found to show low affinity for the relevant peptide, since specific proliferation and IFN-gamma ratios dramatically decreased as L762P peptide was diluted. However, four lines were identified that demonstrated significant activity even at 0.1 micrograms/ml peptide. Each of these lines (referred to as A/D5, D/F5, E/A7 and E/B6) also appeared to specifically proliferate in response to the *E. coli*-derived L762P protein preparation, but not in response to the irrelevant protein preparation. The amino acid sequences of the L762P-derived peptides recognized by these lines are provided in SEQ ID NO: 234, 249, 236 and 245,

respectively. No protein specific IFN-gamma was detected for any of the lines. Lines A/D5, E/A7 and E/B6 were cloned on autologous adherent monocytes pulsed with the relevant peptide at 0.1 (A/D5 and E/A7) or 1 (D/F5) microgram/ml. Following growth, clones were tested for specificity for the relevant peptide. Numerous clones specific for the relevant peptide were identified for lines A/D5 and E/A7.

EXAMPLE 9

PROTEIN EXPRESSION OF LUNG TUMOR-SPECIFIC ANTIGENS

a) Expression of L514S in *E. coli*

The lung tumor antigen L514S (SEQ ID NO: 89) was subcloned into the expression vector pE32b at NcoI and NotI sites, and transformed into *E. coli* using standard techniques. The protein was expressed from residues 3-153 of SEQ ID NO: 89. The expressed amino acid sequence and the corresponding DNA sequence are provided in SEQ ID NO: 252 and 253, respectively.

b) Expression of L762P

Amino acids 32-944 of the lung tumor antigen L762P (SEQ ID NO: 161), with a 6X His Tag, were subcloned into a modified pET28 expression vector, using kanamycin resistance, and transformed into BL21 CodonPlus using standard techniques. Low to moderate levels of expression were observed. The determined DNA sequence of the L762P expression construct is provided in SEQ ID NO: 254.

EXAMPLE 10

IDENTIFICATION OF MHC CLASS II RESTRICTING ALLELE FOR L762P PEPTIDE-SPECIFIC RESPONSES

A panel of HLA mismatched antigen presenting cells (APC) were used to identify the MHC class II restricting allele for the L762P-peptide specific responses of CD4 T cell clones derived from lines that recognized L762P peptide and recombinant protein. Clones from two lines, AD-5 and EA-7, were tested as described below. The

AD-5 derived clones were found to be restricted by the HLA-DRB-1101 allele, and an EA-7 derived clone was found to be restricted by the HLA DRB-0701 or DQB1-0202 allele. Identification of the restriction allele allows targeting of vaccine therapies using the defined peptide to individuals that express the relevant class II allele. Knowing the relevant restricting allele will also enable clinical monitoring for responses to the defined peptide since only individuals that express the relevant allele will be monitored.

CD4 T cell clones derived from line AD-5 and EA-7 were stimulated on autologous APC pulsed with the specific peptide at 10 µg/ml, and tested for recognition of autologous APC (from donor D72) as well as against a panel of APC partially matched with D72 at class II alleles. Table 2 shows the HLA class typing of the APC tested. Adherent monocytes (generated by 2 hour adherence) from four different donors, referred to as D45, D187, D208, and D326, were used as APC in these experiments. Autologous APC were not included in the experiment. Each of the APC were pulsed with the relevant peptide (5a for AD-5 and 3e for 3A-7) or the irrelevant mammoglobin peptide at 10 µg/ml, and cultures were established for 10,000 T cells and about 20,000 APC/well. As shown in Table 3, specific proliferation and cytokine production could be detected only when partially matched donor cells were used as APC. Based on the MHC typing analysis, these results strongly suggest that the restricting allele for the L762-specific response of the AD-5 derived clones is HLA-DRB-1101 and for the EA-7 derived clone the restricting allele is HLA DRB-0701 or DQB1-0202.

Table 2 - HLA Typing of APC

DONOR	DR	DR	DQ	DQ
D72	B1-1101	B1-0701	B1-0202	B1-0301
D45	-3	-15	B1-0201	B1-0602
D187	-4	-15	-1	-7
D208	B1-1101	B1-0407	-3	-3
D326	B1-0301	B1-0701	B1-0202	B1-0201

Table 3 - I.762P Peptide Responses Map to HLA DR Alleles

	AD-5																								EA-7
	A11		B10		C10		C11		E6		F1		F9		G8		G9		G10		G12				
	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN	Prol	γ -IFN			
Donor																									
D72 DR-0701, -1101, DQ-0202, -7	46		31		34		24		31		40		55		45		43		91		10				
D45 DR-3,-15, DQ-1, -0201	32	1.7	5.5	1.2	3.3	1	1.0	1.5	1.1	1.1	1.6	1.1	1.4	1.3	0.2	1.1	1.1	1.1	1.2	1.5	0.8	1.1			
D187 DR-4, -15, DQ-1,-7	14	1.2	1.3	1	1.4	1.1	1.4	1.7	1.0	1.1	1.4	1.2	1.2	1.1	0.9	1	1.0	1	1.0	1.6	0.5	1			
D208 DR-4, -1101, DQ-3	138	13	38	5.4	18.8	10	14.6	4.6	15.3	6.1	45.9	8.6	73.3	14.1	38.0	7.7	174.3	16.1	113.6	19.6	0.8	1			
D326 DR-3, -0701, DQ-0202	0.7	4	0.3	1	0.3	1.4	1.0	2	0.8	1.1	0.3	1.1	0.7	1.1	0.6	1.2	0.4	1	1.2	5	14.1	6.8			

EXAMPLE 11

FUSION PROTEINS OF N-TERMINAL AND C-TERMINAL PORTIONS OF L763P

In another embodiment, a *Mycobacterium tuberculosis*-derived polynucleotide, referred to as Ra12, is linked to at least an immunogenic portion of a polynucleotide of this invention. Ra12 compositions and methods for their use in enhancing expression of heterologous polynucleotide sequences are described in U.S. Patent Application 60/158,585, the disclosure of which is incorporated herein by reference in its entirety. Briefly, Ra12 refers to a polynucleotide region that is a subsequence of a *Mycobacterium tuberculosis* MTB32A nucleic acid. MTB32A is a serine protease of 32 KD molecular weight encoded by a gene in virulent and avirulent strains of *M. tuberculosis*. The nucleotide sequence and amino acid sequence of MTB32A have been described (for example, U.S. Patent Application 60/158,585; see also, Skeiky *et al.*, *Infection and Immun.* (1999) 67:3998-4007, incorporated herein by reference). Surprisingly, it was discovered that a 14 KD C-terminal fragment of the MTB32A coding sequence expresses at high levels on its own and remains as a soluble protein throughout the purification process. Moreover, this fragment may enhance the immunogenicity of heterologous antigenic polypeptides with which it is fused. This 14 KD C-terminal fragment of the MTB32A is referred to herein as Ra12 and represents a fragment comprising some or all of amino acid residues 192 to 323 of MTB32A.

Recombinant nucleic acids which encode a fusion polypeptide comprising a Ra12 polypeptide and a heterologous lung tumor polypeptide of interest, can be readily constructed by conventional genetic engineering techniques. Recombinant nucleic acids are constructed so that, preferably, a Ra12 polynucleotide sequence is located 5' to a selected heterologous lung tumor polynucleotide sequence. It may also be appropriate to place a Ra12 polynucleotide sequence 3' to a selected heterologous polynucleotide sequence or to insert a heterologous polynucleotide sequence into a site within a Ra12 polynucleotide sequence.

In addition, any suitable polynucleotide that encodes a Ra12 or a portion or other variant thereof can be used in constructing recombinant fusion polynucleotides comprising Ra12 and one or more lung tumor polynucleotides disclosed herein.

Preferred Ra12 polynucleotides generally comprise at least about 15 consecutive nucleotides, at least about 30 nucleotides, at least about 60 nucleotides, at least about 100 nucleotides, at least about 200 nucleotides, or at least about 300 nucleotides that encode a portion of a Ra12 polypeptide.

Ra12 polynucleotides may comprise a native sequence (*i.e.*, an endogenous sequence that encodes a Ra12 polypeptide or a portion thereof) or may comprise a variant of such a sequence. Ra12 polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the biological activity of the encoded fusion polypeptide is not substantially diminished, relative to a fusion polypeptide comprising a native Ra12 polypeptide. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native Ra12 polypeptide or a portion thereof.

Two specific embodiments of fusions between Ra12 and antigens of the present invention are described in this example.

A. N-Terminal Portion of L763P

A fusion protein of full-length Ra12 and the N-terminal portion of L763P (referred to as L763P-N; amino acid residues 1-130 of SEQ ID NO: 159) was expressed as a single recombinant protein in *E. coli*. The cDNA for the N-terminal portion was obtained by PCR with a cDNA for the full length L763P and primers L763F3 (5' CGGCGAATTCATGGATTGGGGGACGCTGC; SEQ ID NO: 383) and 1763RV3 (5' CGGCCTCGAGTCAACCCCTCTATCCGAACCTTCTGC; SEQ ID NO: 384). The PCR product with expected size was recovered from agarose gel, digested with restriction enzymes *EcoRI* and *XhoI*, and cloned into the corresponding sites in the expression vector pCRX1. The sequence for the fusion of full-length of Ra12 and L763P-N was confirmed by DNA sequencing. The determined cDNA sequence is provided in SEQ ID NO:351, with the corresponding amino acid sequence being provided in SEQ ID NO: 352).

B. C-Terminal Portion of L763P

A fusion protein of full-length Ra12 and the C-terminal portion of L763P (referred to as L763P-C; amino acid residues 100-262 of SEQ ID NO: 159) was expressed as a single recombinant protein in *E. coli*. The cDNA of the C-terminal portion of L763P was obtained by PCR with a cDNA for the full length of L763P and primers L763F4 (5' CGGCGAATTCCACGAACCACTCGCAAGTTCAG; SEQ ID NO: 385) and L763RV4 (5' CGGCTCGAG-TTAGCTTGCGCCTGTGATTGC; SEQ ID NO: 386). The PCR product with expected size was recovered from agarose gel, digested with restriction enzymes EcoRI and XhoI, and cloned into the corresponding sites in the expression vector pCRX1. The sequence for the fusion of full-length Ra12 and L763P-C was confirmed by DNA sequencing. The determined DNA sequence is provided in SEQ ID NO:353, with the corresponding amino acid sequence being provided in SEQ ID NO: 354.

The recombinant proteins described in this example are useful for the preparation of vaccines, for antibody therapeutics, and for diagnosis of lung tumors.

EXAMPLE 12

EXPRESSION IN *E. COLI* OF L762P HIS TAG FUSION PROTEIN

PCR was performed on the L762P coding region with the following primers:

Forward primer starting at amino acid 32.

PDM-278 5'ggagtacagctcaagacaatggg 3' (SEQ ID NO:355) Tm 57°C.

Reverse primer including natural stop codon after amino acid 920, creating EcoRI site

PDM-280 5'ccatgggaattcattataataattttgttc 3' (SEQ ID NO:356) TM55°C.

The PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The

correct construct was confirmed by DNA sequence analysis and then transformed into BL21 (DE3) pLys S and BL21 (DE3) CodonPlus RIL expression hosts.

The protein sequence of expressed recombinant L762P is shown in SEQ ID NO:357, and the DNA sequence is shown in SEQ ID NO:358.

EXAMPLE 13

EXPRESSION IN *E. COLI* OF A L773PA HIS TAG FUSION PROTEIN

The L773PA coding region (encoding amino acids 2-71 of SEQ ID NO: 172) was PCR amplified using the following primers:

Forward primer for L773PA starting at amino acid 2:

PDM-299 5'tggcagccctctcttcaagtggc 3' (SEQ ID NO:359) Tm63°C.

Reverse primer for L773PA creating artificial stop codon after amino acid 70:

PDM-355 5'cgccagaattcatcaacaatactgttagcacc 3' (SEQ ID NO:360) Tm62°C.

The resulting PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and transformed into BL21 (DE3) pLys S and BL21 (DE3) CodonPlus RIL expression hosts.

The protein sequence of expressed recombinant L773PA is shown in SEQ ID NO:361, and the DNA sequence is shown in SEQ ID NO:362.

EXAMPLE 14

IDENTIFICATION OF EPITOPES DERIVED FROM LUNG TUMOR SPECIFIC POLYPEPTIDES

A series of peptides from the L773P amino acid sequence (SEQ ID NO: 172) were synthesized and used in *in vitro* priming experiments to generate peptide-specific CD4 T cells. These peptides were 20-mers that overlapped by 15 amino acids and corresponded to amino acids 1-69 of the L773P protein. This region has been demonstrated to be tumor-specific. Following three *in vitro* stimulations, CD4 T cell

lines were identified that produced IFN γ in response to the stimulating peptide but not the control peptide. Some of these T cell lines demonstrated recognition of recombinant L773P and L773PA (tumor-specific region) proteins.

To perform the experiments, a total of eleven 20-mer peptides (SEQ ID NO: 363, 365 and 387-395) overlapping by 15 amino acids and derived from the N-terminal tumor-specific region of L773P (corresponding to amino acids 1-69 of SEQ ID NO:172) were generated by standard procedures. Dendritic cells were derived from PBMC of a normal donor using GM-CSF and IL-4 by standard protocol. Purified CD4 T cells were generated from the same donor as the dendritic cells using MACS beads and negative selection of PBMCs. Dendritic cells were pulsed overnight with the individual 20-mer peptides at a concentration of 10 μ g/ml. Pulsed dendritic cells were washed and plated at 1×10^4 /well of a 96-well U-bottom plates, and purified CD4 cells were added at 1×10^5 well. Cultures were supplemented with 10 ng/ml IL-6 and 5 ng/ml IL-12, and incubated at 37°C. Cultures were re-stimulated as above on a weekly basis using as APC dendritic cells generated and pulsed as above, supplemented with 5 ng/ml IL-7 and 10 μ g/ml IL-2. Following 3 *in vitro* stimulation cycles, cell lines (each corresponding to one well) were tested for cytokine production in response to the stimulating peptide vs. an irrelevant peptide.

A small number of individual CD4 T cell lines (9/528) demonstrated cytokine release (IFN γ) in response to the stimulating peptide but not to control peptide. The CD4 T cell lines that demonstrated specific activity were restimulated on the appropriate L773P peptide and reassayed using autologous dendritic cells pulsed with 10 μ g/ml of the appropriate L773P peptide, an irrelevant control peptide, recombinant L773P protein (amino acids 2-364, made in *E. coli*), recombinant L773PA (amino acids 2-71, made in *E. coli*), or an appropriate control protein (L3E, made in *E. coli*). Three of the nine lines tested (1-3C, 1-6G, and 4-12B) recognized the appropriate L773P peptide as well as recombinant L773P and L773PA. Four of the lines tested (4-8A, 4-8E, 4-12D, and 4-12E) recognized the appropriate L773P peptide only. Two of the lines tested (5-6F and 9-3B) demonstrated non-specific activity.

These results demonstrate that the peptide sequences MWQPLFFKWLSCCPGSSQI (amino acids 1-20 of SEQ ID NO: 172; SEQ ID NO:363) and GSSQIAAAASTQPEDDINTQ (amino acids 16-35 of SEQ ID NO: 172;

SEQ ID NO: 365) may represent naturally processed epitopes of L773P, which are capable of stimulating human class II MHC-restricted CD4 T cell responses.

In subsequent studies, the above epitope mapping experiment was repeated using a different donor. Again, some of the resulting T cell lines were found to respond to peptide and recombinant protein. An additional peptide was found to be naturally processed. Specifically, purified CD4 cells were stimulated on a total of eleven 20-mer peptides overlapping by 15 amino acids (SEQ ID NO: 363, 387, 388, 365 and 389-395, respectively). The priming was carried out as described above, except that a peptide concentration of 0.5 ug/mL rather than 10 ug/mL was employed. In the initial screen of the cell lines 9 of the 528 lines released at least a three-fold greater level of IFN-gamma with stimulating peptide vs. control peptide. These 9 lines were restimulated on the appropriate peptide and then tested on dendritic cells pulsed with a titration of appropriate peptide (10 ug/mL, 1 ug/mL and 0.1 ug/mL), and 10 ug/mL of a control peptide. Six of the 9 lines recognized recombinant L773P as well as peptide. The six lines referred to as 1-1E, 1-2E, 1-4H, 1-6A, 1-6G and 2-12B recognized L773PA and the appropriate peptide. These results demonstrate that the peptides of SEQ ID NO: 363 and 387 represent naturally processed epitopes of L773P.

Using the procedures described above, CD4+ T cell responses were generated from PBMC of normal donors using dendritic cells pulsed with overlapping 20-mer peptides (SEQ ID NO: 396-419) spanning the L523S polypeptide sequence (SEQ ID NO: 176). A number of CD4+ T cells demonstrated reactivity with the priming peptides as well as with L523S recombinant protein, with the dominant reactivity of these lines being within the peptides 4, 7 and 21 (SEQ ID NO: 399, 402 and 416; corresponding to amino acids 30-39, 60-79 and 200-219, respectively, of SEQ ID NO: 176).

Epitopes within the scope of the invention include epitopes restricted by other class II MHC molecules. In addition, variants of the peptide can be produced wherein one or more amino acids are altered such that there is no effect on the ability of the peptides to bind to MHC molecules, no effect on their ability to elicit T cell responses, and no effect on the ability of the elicited T cells to recognize recombinant protein.

EXAMPLE 15

SURFACE EXPRESSION OF L762P AND ANTIBODY EPITOPES THEREOF

Rabbits were immunized with full-length histidine-tagged L762P protein generated in *E. coli*. Sera was isolated from rabbits and screened for specific recognition of L762P in ELISA assays. One polyclonal serum, referred to as 2692L, was identified that specifically recognized recombinant L762P protein. The 2692L anti-L762P polyclonal antibodies were purified from the serum by affinity purification using L762P affinity columns. Although L762P is expressed in a subset of primary lung tumor samples, expression appears to be lost in established lung tumor cell lines. Therefore, to characterize surface expression of L762P, a retrovirus construct that expresses L762P was used to transduce primary human fibroblasts as well as 3 lung tumor cell lines (522-23, HTB, and 343T). Transduced lines were selected and expanded to examine L762P surface expression by FACS analysis. For this analysis, non-transduced and transduced cells were harvested using cell dissociation medium, and incubated with 10-50 micrograms/ml of either affinity purified anti-L762P or irrelevant antisera. Following a 30 minute incubation on ice, cells were washed and incubated with a secondary, FITC conjugated, anti rabbit IgG antibody as above. Cells were washed, resuspended in buffer with Propidium Iodide (PI) and examined by FACS using an Excalibur fluorescence activated cell sorter. For FACS analysis, PI-positive (i.e. dead/permeabilized cells) were excluded. The polyclonal anti-L762P sera specifically recognized and bound to the surface of L762P-transduced cells but not the non-transduced counterparts. These results demonstrate that L762P is localized to the cell surface of both fibroblasts as well as lung tumor cells.

To identify the peptide epitopes recognized by 2692L, an epitope mapping approach was pursued. A series of overlapping 19-21 mers (5 amino acid overlap) was synthesized that spanned the C terminal portion of L762P (amino acids 481-894 of SEQ ID NO: 161). In an initial experiment peptides were tested in pools. Specific reactivity with the L762P antiserum was observed with pools A, B, C, and E. To identify the specific peptides recognized by the antiserum, flat bottom 96 well microtiter plates were coated with individual peptides at 10 microgram/ml for 2 hours at

37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 5% (w/v) milk for 2 hours at 37 °C, and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit anti-L762P serum 2692L was added at 200 or 20 ng/well to triplicate wells in PBST and incubated overnight at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti rabbit IgG (H+L) Affinipure F(ab') fragment at 1:2,000 for 60 minutes. Plates were then washed, and incubated in tetramethyl benzidine substrate. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450/570 nm using an ELISA plate reader.

The resulting data, presented in Table 4 below, demonstrates that the L762P antisera recognized at least 6 distinct peptide epitopes from the 3' half of L762P.

Table 4

ELISA activity (OD 450-570)

Peptide (starting amino acid of L762P)	pool	200 ng polyclonal serum	20 ng polyclonal serum
A (481)	A	1.76	1.0
B (495)	A	0.14	.06
C (511)	E	0.47	0.18
D (526)	E	0.11	0.09
E (541)	A	0.11	0.04
F (556)	A	0.04	0.02
G (571)	A	0.06	0.02
H (586)	B	0.1	0.03
I (601)	B	0.25	0.06
J (616)	B	0.1	0.03
K (631)	E	0.1	0.08
L (646)	B	0.28	0.12
M (661)	B	0.14	0.03
N (676)	C	0.12	0.1
O (691)	C	1.1	0.23
P (706)	C	0.1	0.03
Q (721)	C	0.11	0.05
R (736)	E	0.12	0.04
S (751)	C	0.15	0.06
U (781)	D	0.12	0.06
V (795)	F	0.07	0.05
X (826)	D	0.1	0.03
Y (841)	D	0.17	0.07
Z (856)	D	0.16	0.08
AA (871)	F	0.17	0.05
BB (874)	F	0.14	0.11
No peptide		0.15	0.045

Individual peptides were identified from each of the pools, and additionally a weak reactivity was identified with peptide BB from pool F. The relevant peptide epitopes are summarized in the Table 5 below. The amino acid sequences for peptides BB, O, L, I, A and C are provided in SEQ ID NO: 376-381, respectively, with the corresponding cDNA sequences being provided in SEQ ID NO: 373, 370, 372, 374, 371 and 375, respectively.

Table 5
ELISA activity
(OD 450-570)

Peptide	Nucleotides of L762P	Amino acids of L762P	Sequence	pool	200 ng	20 ng
A	1441-1500	481-500	SRSSGTGDIFQQHIQLEST	A	1.76	1.0
C	1531-1590	511-530	KNTVTVDNTVGNDTMFLVTW	E	0.47	0.18
I	1801-1860	601-620	AVPPATVEAFVERDSLHFP	B	0.25	0.06
L	1936-1955	646-665	PETGDPVTLRLDDGAGADV	B	0.28	0.12
O	2071-2130	691-710	VNHSPSISTPAHSIPGSHAMIL	C	1.1	0.23
BB	2620-2679	874-893	LQSAVSNIQAPLFIPFNSD	F	0.14	0.11
None	-	-	-	-	0.15	0.05

EXAMPLE 16

DETECTION OF ANTIBODIES AGAINST LUNG TUMOR ANTIGENS IN PATIENT SERA

Antibodies specific for the lung tumor antigens L773PA (SEQ ID NO:361), L514S (SEQ ID NO:155 and 156), L523S (SEQ ID NO:176), L762P (SEQ ID NO:161) and L763P (SEQ ID NO:159) were shown to be present in effusion fluid or sera of lung cancer patients but not in normal donors. More specifically, the presence of antibodies against L773PA, L514S, L523S, L762P and L763P in effusion fluid obtained from lung cancer patients and in sera from normal donors was detected by ELISA using recombinant proteins and HRP-conjugated anti-human Ig. Briefly, each protein (100 ng) was coated in 96-well plate at pH 9.5. In parallel, BSA (bovine serum albumin) was also coated as a control protein. The signals ([S], absorbance measured at 405 nm) against BSA ([N]) were determined. The results of these studies are shown in Table 6, wherein - represents [S]/[N] < 2; +/- represents [S]/[N] > 2; ++ represents [S]/[N] > 3; and +++ represents [S]/[N] > 5.

Table 6

Detection of Antibodies Against Lung Tumor Antigens

	L514S	L523S	L762P	L763P	L773PA
Effusion fluid					
#1	+++	++	++	-	++
#2	-	-	+/-	++	+/-
#3	-	-	-	-	+/-
#4	+/-	++	+/-	-	+/-
#5	+/-	+++	+/-	+/-	++
#7	-	+/-	-	-	+/-
#8	-	+++	-	-	++
#10	-	++	+/-	+/-	-
#11	+/-	++	++	-	++
#12	+++	+/-	-	+/-	+/-
#13	-	+/-	-	-	+/-
#14	-	+++	+/-	+/-	++
#15	+/-	++	+/-	-	++
#17	-	+/-	-	-	+/-
#18	-	++	-	-	-
#19	-	+/-	-	-	+/-
#20	+/-	+/-	+/-	-	+/-
Normal sera					
#21	-	+/-	-	-	-
#22	-	-	-	-	-
#23	-	-	-	-	+/-
#24	-	+/-	-	-	-
#25	+/-	+/-	-	-	+/-

Using Western blot analyses, antibodies against L523S were found to be present in 3 out of 4 samples of effusion fluid from lung cancer patients, with no L523S antibodies being detected in the three samples of normal sera tested.

EXAMPLE 17

EXPRESSION IN *E. COLI* OF A L514S HIS TAG FUSION PROTEIN

PCR was performed on the L514S-13160 coding region with the following primers:

Forward primer PDM-278 5' cacactagtgtccgcgtggcgcgcctac 3' (SEQ ID NO:421) Tm 67°C.

Reverse primer PDM-280 5' catgagaattcatcacatgccctgaaggtccc 3'
(SEQ ID NO:422) TM 66°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 66°C for 15 seconds, 72°C for 1 minute with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into BL21 CodonPlus (Stratagene, La Jolla, CA) cells for expression.

The amino acid sequence of expressed recombinant L514S is shown in SEQ ID NO:423, and the DNA coding region sequence is shown in SEQ ID NO:424.

EXAMPLE 18

EXPRESSION IN *E. COLI* OF A L523S HIS TAG FUSION PROTEIN

PCR was performed on the L523S coding region with the following primers:

Forward primer PDM-414 5' aacaaactgtatatcggaaacctcagcgagaa 3' (SEQ ID NO:425) Tm 62°C.

Reverse primer PDM-415 5' ccatagaattcattactccgtcttgactgagg 3' (SEQ ID NO:426) TM 62°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 62°C for 15 seconds, 72°C for 4 minutes with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into BL21 CodonPlus (Stratagene, La Jolla, CA) cells for expression.

The amino acid sequence of expressed recombinant L523S is shown in SEQ ID NO:427, and the DNA coding region sequence is shown in SEQ ID NO:428.

EXAMPLE 19

EXPRESSION IN *E. COLI* OF A L762PA HIS TAG FUSION PROTEIN

PCR was performed on the L762PA coding region (L762PA is missing the signal sequence, the C-terminal transmembrane domain and the cytoplasmic tail) with the following primers:

Forward primer PDM-278 5'ggagtacagcttcaagacaatggg 3' (SEQ ID NO:355) Tm 57°C.

Reverse primer PDM-279 5'ccatggaattcattatttcaatataagataatctc 3' (SEQ ID NO:429) TM56°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 55°C for 15 seconds, 72°C for 5 minutes with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into BL21 pLys S (Novagen, Madison, WI) cells for expression.

The amino acid sequence of expressed recombinant L762PA is shown in SEQ ID NO:430, and the DNA coding region sequence is shown in SEQ ID NO:431.

EXAMPLE 20

EXPRESSION IN *E. COLI* OF A L773P HIS TAG FUSION PROTEIN

PCR was performed on the L773P coding region with the following primers:

Forward primer PDM-299 5' tggcagccctcttcttcaagtggc 3' (SEQ ID NO:359) Tm 63°C.

Reverse primer PDM-300 5' cgctgtctgcagtcattaattcatcagaaaatgg 3' (SEQ ID NO:432) TM 63°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 63°C for 15 seconds, 72°C for 2 minutes 15 seconds with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with EcoRI restriction enzyme, gel purified and then cloned into pPDM His, a modified pET28 vector with a His tag in frame, which had been digested with Eco72I and EcoRI restriction enzymes. The

correct construct was confirmed by DNA sequence analysis and then transformed into BL21 pLys S (Novagen, Madison, WI) and BL21 CodonPlus (Stratagene, La Jolla, CA) cells for expression.

The amino acid sequence of expressed recombinant L773P is shown in SEQ ID NO:433, and the DNA coding region sequence is shown in SEQ ID NO:434.

EXAMPLE 21

CLONING AND SEQUENCING OF A T-CELL RECEPTOR CLONE FOR THE LUNG SPECIFIC ANTIGEN L762P

T cell receptor (TCR) alpha and beta chains from a CD4 T cell clone specific for the lung specific antigen L762P were cloned and sequence. Basically, total mRNA from 2×10^6 cells from CTL clone 4H6 was isolated using Trizol reagent and cDNA was synthesized using Ready-to go kits (Pharmacia). To determine Valpha and Vbeta sequences of this clone, a panel of Valpha and Vbeta subtype specific primers was synthesized and used in RT-PCR reactions with cDNA generated from each of the clones. The RT-PCR reactions demonstrated that each of the clones expressed a common Vbeta sequence that corresponded to the Vbeta8 subfamily and a Valpha sequence that corresponded to the Valpha8 subfamily. To clone the full TCR alpha and beta chains from clone 4H6, primers were designed that spanned the initiator and terminator-coding TCR nucleotides. The primers were as follows:

forward primer for TCR Valpha8 5'
ggatccgcccaccatgacatccattcgagctgta 3' (SEQ ID NO:435; has a BamHI site inserted);

Kozak reverse primer for TCR Valpha8 (antisense) 5'
gtcgactcagctggaccacagccgag 3' (SEQ ID NO:436; has a SalI site inserted plus the TCR alpha constant sequence);

forward primer for TCR Vbeta8 (sense) 5'
ggatccgcccaccatggactcctggaccttctgct 3' (SEQ ID NO:437; has a BamHI site inserted); and

Kozak reverse primer for TCR Vbeta 5' gtcgactcagaatctttctcttgac 3'
(SEQ ID NO:438; has a SalI site inserted plus the TCR beta constant sequence).

Standard 35 cycle RT-PCR reactions were established using the cDNA synthesized from the CTL clone and the above primers utilizing the proofreading thermostable polymerase, PWO (Roche). The resultant PCR band, about 850 bp for Valpha and about 950 for Vbeta, was ligated into a PCR blunt vector (Invitrogen) and transformed into *E. coli*. *E. coli* transformed with plasmids having full-length alpha and beta chains were identified.. Large scale preparations of the corresponding plasmids were generated, and these plasmids were sequenced. The Valpha sequence (SEQ ID NO:439) was shown by nucleotide sequence alignment to be homologous to Valpha8.1, while the Vbeta sequence (SEQ ID NO:440) was shown by nucleotide sequence alignment to be homologous to Vbeta8.2.

EXAMPLE 22

RECOMBINANT EXPRESSION OF FULL LENGTH L762P IN MAMMALIAN CELLS

Full length L762P cDNA was subcloned into the mammalian expression vectors VR1012 and pCEP4 (Invitrogen). Both expression vectors had previously been modified to contain a FLAG epitope tag. These constructs were transfected into HEK293 and CHL-1 cells (ATCC) using Lipofectamine 2000 reagent (Gibco). Briefly, both the HEK and CHL-1 cells were plated at a density of 100,000 cells/ml in DMEM (Gibco) containing 10% FBS (Hyclone) and grown overnight. The following day, 4µl of Lipofectamine 2000 was added to 100µl of DMEM containing no FBS and incubated for 5 minutes at room temperature. The Lipofectamine/DMEM mixture was then added to 1µg of L762P Flag/pCEP4 or L762P Flag/VR1012 plasmid DNA resuspended in 100µl DMEM and incubated for 15 minutes at room temperature. The Lipofectamine/DNA mix was then added to the HEK293 and CHL-1 cells and incubated for 48-72 hours at 37°C with 7% CO₂. Cells were rinsed with PBS, then collected and pelleted by centrifugation. L762P expression was detected in the transfected HEK293 and CHL-1 cell lysates by Western blot analysis and was detected on the surface of transfected HEK cells by flow cytometry analysis.

For Western blot analysis, whole cell lysates were generated by incubating the cells in Triton-X100 containing lysis buffer for 30 minutes on ice. Lysates were then cleared by centrifugation at 10,000 rpm for 5 minutes at 4°C. Samples were diluted with SDS-PAGE loading buffer containing beta-mercaptoethanol, then boiled for 10 minutes prior to loading the SDS-PAGE gel. The protein was transferred to nitrocellulose and probed using 1 µg/ml purified anti-L762P rabbit polyclonal sera (lot #690/73) or non-diluted anti-L762P mAb 153.20.1 supernatant. Blots were revealed using either goat anti-rabbit Ig coupled to HRP or goat anti-mouse Ig coupled to HRP followed by incubation in ECL substrate.

For flow cytometric analysis, cells were washed further with ice cold staining buffer (PBS+1%BSA +Azide). Next, the cells were incubated for 30 minutes on ice with 10ug/ml of purified anti-L762P polyclonal sera (lot #690/73) or a 1:2 dilution of anti-L762P mAb 153.20.1 supernatant. The cells were washed 3 times with staining buffer and then incubated with a 1:100 dilution of goat anti-rabbit Ig(H+L)-FITC or goat anti-mouse Ig(H+L)-FITC reagent (Southern Biotechnology) for 30 minutes on ice. After 3 washes, the cells were resuspended in staining buffer containing propidium iodide (PI), a vital stain that allows for the exclusion of permeable cells, and analyzed by flow cytometry.

EXAMPLE 23

GENERATION OF POLYCLONAL ANTIBODIES TO LUNG TUMOR ANTIGENS

Three lung antigens, L523S (SEQ ID NO:176), L763P (SEQ ID NO:159) and L763 peptide #2684 (SEQ ID NO:441), were expressed and purified for use in antibody generation.

L523S and L763P were expressed in an *E. coli* recombinant expression system and grown overnight in LB Broth with the appropriate antibiotics at 37°C in a shaking incubator. The next morning, 10 ml of the overnight culture was added to 500 ml of 2x YT with the appropriate antibiotics in a 2L-baffled Erlenmeyer flask. When the optical density of the culture reached 0.4-0.6 at 560 nanometers, the cells were

induced with IPTG (1 mM). Four hours after induction with IPTG, the cells were harvested by centrifugation.

The cells were then washed with phosphate buffered saline and centrifuged again. The supernatant was discarded and the cells were either frozen for future use or immediately processed. Twenty milliliters of lysis buffer was added to the cell pellets and vortexed. To break open the *E. coli* cells, this mixture was then run through a french press at a pressure of 16,000 psi. The cells were then centrifuged again and the supernatant and pellet were checked by SDS-PAGE for the partitioning of the recombinant protein.

For proteins that localized to the cell pellet, the pellet was resuspended in 10 mM Tris pH 8.0, 1% CHAPS and the inclusion body pellet was washed and centrifuged again. This procedure was repeated twice more. The washed inclusion body pellet was solubilized with either 8M urea or 6M guanidine HCl containing 10 mM Tris pH 8.0 plus 10 mM imidazole. The solubilized protein was added to 5 ml of nickel-chelate resin (Qiagen) and incubated for 45 minutes to 1 hour at room temperature with continuous agitation.

After incubation, the resin and protein mixture was poured through a disposable column and the flow through was collected. The column was then washed with 10-20 column volumes of the solubilization buffer. The antigen was then eluted from the column using 8M urea, 10 mM Tris pH 8.0 and 300 mM imidazole and collected in 3 ml fractions. A SDS-PAGE gel was run to determine which fractions to pool for further purification.

As a final purification step, a strong anion exchange resin, in this case Hi-Prep Q (Biorad), was equilibrated with the appropriate buffer and the pooled fractions from above were loaded onto the column. Each antigen was eluted off the column with an increasing salt gradient. Fractions were collected as the column was run and another SDS-PAGE gel was run to determine which fractions from the column to pool.

The pooled fractions were dialyzed against 10 mM Tris pH 8.0. The release criteria were purity as determined by SDS-PAGE or HPLC, concentration as determined by Lowry assay or Amino Acid Analysis, identity as determined by amino

terminal protein sequence, and endotoxin level was determined by the Limulus (LAL) assay. The proteins were then put in vials after filtration through a 0.22-micron filter and the antigens were frozen until needed for immunization.

The L763 peptide #2684 was synthesized and conjugated to KLH and froze until needed for immunization.

The polyclonal antisera were generated using 400 micrograms of each lung antigen combined with 100 micrograms of muramyl dipeptide (MDP). An equal volume of Incomplete Freund's Adjuvant (IFA) was added and then mixed and injected subcutaneously (S.C.) into a rabbit. After four weeks, the rabbit was S.C. boosted with 200 micrograms of antigen mixed with an equal volume of IFA. Thereafter the rabbit was I.V. boosted with 100 micrograms of antigen. The animal was bled seven days following each boost. The blood was then incubated at 4°C for 12-24 hours followed by centrifugation to generate the sera.

The polyclonal antisera were characterized using 96 well plates coated with antigen and incubated with 50 microliters (typically 1 microgram/microliter) of the polyclonal antisera at 4°C for 20 hours. Basically, 250 microliters of BSA blocking buffer was added to the wells and incubated at room temperature for 2 hours. Plates were washed 6 times with PBS/0.1% Tween. The rabbit sera were diluted in PBS/0.1% Tween/0.1%BSA. 50 microliters of diluted sera was added to each well and incubated at room temperature for 30 minutes. The plates were washed as described above, and then 50 microliters of goat anti-rabbit horseradish peroxidase (HRP) at a 1:10000 dilution was added and incubated at room temperature for 30 minutes.

The plates were washed as described above, and 100 microliters of TMB Microwell Peroxidase Substrate was added to each well. Following a 15-minute incubation in the dark at room temperature, the colorimetric reaction was stopped with 100 microliters of 1N H₂SO₄ and read immediately at 450 nm. All the polyclonal antibodies showed immunoreactivity to the appropriate antigen. Tables 7-9 show the antibody reactivity of rabbit antisera in serial dilution to the three lung antigens, L523S, L763P and L763 peptide #2684. The first column shows the antibody dilutions. The columns "Pre-immune sera" indicate ELISA data for two experiments using pre-immune sera. These results are averaged in the fourth column. The columns "anti-

L523S, L763P or #2684" indicate ELISA data for two experiments using sera from rabbits immunized as described in this Example, using the respective antigen, referred to as either L523S, L763P or #2684 in the tables.

Table 7

Antibody dilution	Pre-immune sera (1)	Pre-immune sera (2)	Average	Anti-L523S (1)	Anti-L523S (2)	Average
1:1000	0.14	0.14	0.14	2.36	2.37	2.37
1:2000	0.12	0.10	0.11	2.29	2.23	2.26
1:4000	0.10	0.09	0.10	2.11	2.17	2.14
1:8000	0.09	0.09	0.09	1.98	2.00	1.99
1:16000	0.09	0.09	0.09	1.73	1.76	1.75
1:32000	0.09	0.09	0.09	1.35	1.40	1.37
1:64000	0.09	0.11	0.10	0.94	0.98	0.96
1:128000	0.09	0.08	0.08	0.61	0.61	0.61
1:256000	0.08	0.08	0.08	0.38	0.38	0.38
1:512000	0.09	0.08	0.08	0.24	0.25	0.25
1:1024000	0.08	0.08	0.08	0.17	0.17	0.17
1:2048000	0.08	0.08	0.08	0.14	0.13	0.13

Table 8

Antibody dilution	Pre-immune sera (1)	Pre-immune sera (2)	Average	Anti-L763P (1)	Anti-L763P (2)	Average
1:1000	0.09	0.11	0.10	1.97	1.90	1.93
1:2000	0.07	0.07	0.07	1.86	1.84	1.85
1:4000	0.06	0.06	0.06	1.82	1.81	1.81
1:8000	0.06	0.06	0.06	1.83	1.81	1.82
1:16000	0.06	0.05	0.06	1.79	1.74	1.76
1:32000	0.06	0.06	0.06	1.56	1.51	1.53
1:64000	0.06	0.05	0.05	1.35	1.34	1.35
1:128000	0.05	0.05	0.05	1.01	0.98	0.99
1:256000	0.06	0.05	0.05	0.69	0.70	0.70
1:512000	0.06	0.05	0.05	0.47	0.44	0.46
1:1024000	0.06	0.05	0.06	0.27	0.27	0.27
1:2048000	0.05	0.05	0.05	0.16	0.15	0.16

Table 9

Antibody dilution	Pre-immune sera (1)	Pre-immune sera (2)	Average	Anti-#2684 (1)	Anti-#2684 (2)	Average
1:1000	0.07	0.07	0.07	2.10	2.00	2.05
1:2000	0.07	0.06	0.06	1.95	1.96	1.95
1:4000	0.06	0.06	0.06	1.77	1.82	1.79
1:8000	0.06	0.06	0.06	1.79	1.81	1.80
1:16000	0.06	0.06	0.06	1.54	1.50	1.52
1:32000	0.06	0.06	0.06	1.27	1.20	1.24
1:64000	0.06	0.06	0.06	0.85	0.82	0.83
0	0.06	0.06	0.06	0.06	0.06	0.06

Tables 10-12 show the affinity purification of the respective antibodies to the three lung antigens, L523S, L763P and L763 peptide #2684.

Table 10

Antibody conc. (µg/ml)	Affinity pure (salt peak)	Affinity pure (salt peak)	Average	Affinity pure (acid peak)	Affinity pure (acid peak)	Average
1.0	2.38	2.35	2.36	2.25	2.31	2.28
0.5	2.24	2.22	2.23	2.19	2.18	2.18
0.25	2.05	2.09	2.07	2.01	2.03	2.02
0.13	1.70	1.81	1.75	1.74	1.74	1.74
0.063	1.44	1.44	1.44	1.43	1.38	1.40
0.031	1.05	1.05	1.05	0.99	0.99	0.99
0.016	0.68	0.67	0.68	0.65	0.64	0.64
0.0078	0.43	0.42	0.42	0.39	0.39	0.39
0.0039	0.27	0.26	0.27	0.24	0.26	0.25
0.0020	0.18	0.20	0.19	0.19	0.18	0.19
0.0010	0.13	0.14	0.13	0.13	0.14	0.13
0.00	0.11	0.12	0.11	0.10	0.12	0.11

Table 11

Antibody dilution	Affinity pure	Affinity pure	Average
1:1000	1.64	1.77	1.70
1:2000	1.59	1.76	1.68
1:4000	1.48	1.62	1.55
1:8000	1.35	1.43	1.39
1:16000	1.09	1.19	1.14
1:32000	0.81	0.89	0.85
1:64000	0.55	0.58	0.56
1:128000	0.31	0.35	0.33
1:256000	0.18	0.20	0.19
1:512000	0.11	0.12	0.11
1:1024000	0.07	0.07	0.07
1:2048000	0.06	0.06	0.06

Table 12

Antibody conc. (µg/ml)	Affinity pure	Affinity pure	Average
1.0	2.00	2.02	2.01
0.5	2.01	1.93	1.97
0.25	1.84	1.83	1.84
0.13	1.80	1.83	1.81
0.06	1.39	1.60	1.50
0.03	1.33	1.35	1.34
0.02	0.94	0.93	0.94
0.00	0.06	0.06	0.06

EXAMPLE 24**FULL-LENGTH cDNA SEQUENCE ENCODING L529S**

The isolation of a partial sequence (SEQ ID NO:106) for lung antigen L529S was previously provided in Example 2. This partial sequence was used as a query to identify potential full length cDNA and protein sequences by searching against publicly available databases. The predicted full-length cDNA sequence for the isolated

cloned sequence of SEQ ID NO:106 is provided in SEQ ID NO:442. The deduced amino acid sequence of the antigen encoded by SEQ ID NO:442 is provided in SEQ ID NO:443. It was previously disclosed in Example 2 that L529S shows similarity to connexin 26, a gap junction protein.

EXAMPLE 25

EXPRESSION IN MEGATERIUM OF A HISTIDINE TAG-FREE L523S FUSION PROTEIN

PCR was performed on the L523S coding region with the following primers:

Forward primer PDM-734 5' caatcagcgcacacacaactgtatatcggaac 3' (SEQ ID NO:444) Tm 63°C.

Reverse primer PDM-735 5' cgtaagatcttcattactccgtcttgac 3' (SEQ ID NO:445) TM 60°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 62°C for 15 seconds, 72°C for 4 minutes with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with SphI and BglII restriction enzymes, gel purified and then cloned into pMEG-3, which had been digested with SphI and BglII restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into Megaterium cells for expression.

The amino acid sequence of expressed recombinant L523S is shown in SEQ ID NO:446, and the DNA coding region sequence is shown in SEQ ID NO:447.

EXAMPLE 26

EXPRESSION IN *E. COLI* OF A HISTIDINE TAG-FREE L523S FUSION PROTEIN

PCR was performed on the L523S coding region with the following primers:

Forward primer PDM-733 5' cgtactagcatatgaacaaactgtatatcggaac 3' (SEQ ID NO:448) Tm 64°C.

Reverse primer PDM-415 5' ccatagaattcattactccgtcttgactgagg 3' (SEQ ID NO:426) TM 62°C.

The PCR conditions were as follows:

10µl 10X Pfu buffer

1.0µl 10mM dNTPs

2.0µl 10µM each primer

83µl sterile water

1.5µl Pfu DNA polymerase (Stratagene, La Jolla, CA)

50ng DNA

96°C for 2 minutes, 96°C for 20 seconds, 62°C for 15 seconds, 72°C for 4 minute with 40 cycles and then 72°C for 4 minutes.

The PCR product was digested with NdeI and EcoRI restriction enzymes, gel purified and then cloned into pPDM, a modified pET28 vector, which had been digested with NdeI and EcoRI restriction enzymes. The correct construct was confirmed by DNA sequence analysis and then transformed into BLR pLys S and HMS 174 pLys S cells for expression.

The amino acid sequence of expressed recombinant L523S is shown in SEQ ID NO:449, and the DNA coding region sequence is shown in SEQ ID NO:450.

EXAMPLE 27

EPITOPE-ANALYSIS OF L514S AND L523S-SPECIFIC ANTIBODIES

Peptides of candidate antigens can be used for the evaluation of antibody responses in both preclinical and clinical studies. These data allow one to further

confirm the antibody response against a certain candidate antigen. Protein-based ELISA with and without competitive peptides and peptide-based ELISA can be used to evaluate these antibody responses. Peptide ELISA is especially useful since it can further exclude the false positive of the antibody titer observed in protein-based ELISA as well as to provide the simplest assay system to test antibody responses to candidate antigens. In this example, data was obtained using both L514S- and L523S-peptides that show that individual cancer patients produce L514S- and L523S-specific antibodies. The L514S-specific antibodies recognize primarily the following epitope of L514S:

aa86-110: LGKEVRDAKITPEAFEKLGFPAAKE (SED ID NO:451).

This epitope is the common epitope in humans. A rabbit antibody specific for L514S recognizes two addition epitopes of L514S:

(1) aa21-45: KASDGDYYTLAVPMGDVPMGDGISA (SEQ ID NO:452)

(2) aa121-135: PDRDVNLTHQLNPKVK (SED ID NO:453)

It was further found that the SEQ ID NO:452 is common to both L514S isoforms, L514S-13160 and L514S-13166, whereas the other epitopes, SEQ ID NO:451 and SEQ ID NO:453, are probably specific to the isoform, L514S-13160.

The L523S-specific antibodies recognize primarily the following epitope of L523S:

aa440-460: KIAPAEAPDAKVRMVITGP (SEQ ID NO:454).

This epitope is the common epitope in humans. A rabbit antibody specific for L523S recognizes two other epitopes:

(1) aa156-175 PDGAAQQNNPLQQPRG (SEQ ID NO:455)

(2) aa326-345: RTITVKGNVETCAKAEIEIM (SED ID NO:456)

In further studies, it was determined by peptide based ELISAs that eight additional epitopes of L523S were recognized by L523S-specific antibodies:

(1) aa40-59	AFVDCPDESWALKAIEALS	(SEQ	ID
	NO:457)		
(2) aa80-99:	IRKLQIRNIPPHLQWEVLDS	(SED	ID
	NO:458)		
(3) aa160-179:	AQQNPLQQPRGRRGLGQRGS	(SEQ	ID
	NO:459)		
(4) aa180-199:	DVHRKENAGAAEKSITILST	(SED	ID
	NO:460)		
(5) aa320-339:	LYNPRTITTVKGNVETCAKA	(SEQ	ID
	NO:461)		
(6) aa340-359:	EEEIMKKIRESYENDIASMN	(SED	ID
	NO:462)		
(7) aa370-389:	LNALGLFPPTSGMPPPTSGP	(SEQ	ID
	NO:463)		
(8) aa380-399:	KIAPAEAPDAKVRMVIITGP	(SED	ID
	NO:464)		

Out of these, six epitopes are common in both lung plural effusion fluid samples and in sera of lung patients. Of these six, SEQ ID NO:459 and SEQ ID NO:463 have no homology to other L523S-family proteins such as IGF-II mRNA-binding proteins 1 and 2. Accordingly, this indicates that these two peptides can be used as an assay system to determine the antibody response to L523S.

EXAMPLE 28

GENERATION OF L523S-SPECIFIC CTL LINES USING IN VITRO WHOLE-GENE PRIMING

To determine if L523S is capable of generating a CD8⁺ T cell immune response, CTLs were generated using *in vitro* whole-gene priming methodologies with tumor antigen-vaccinia infected DC (Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with the L552S tumor antigen, as determined by interferon-gamma ELISPOT analysis. Specifically, dendritic cells (DC) were

differentiated from Percoll-purified monocytes derived from PBMC of normal human donors by plastic adherence and growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following the five days of culture, the DC were infected overnight with a recombinant adenovirus that expresses L523S at a multiplicity of infection (M.O.I) of 33, 66 and 100, and matured overnight by the addition of 2 µg/ml CD40 ligand. The virus was then inactivated by UV irradiation. In order to generate a CTL line, autologous PBMC were isolated and CD8+ T cells were enriched for by the negative selection using magnetic beads conjugated to CD4+, CD14+, CD16+, CD19+, CD34+ and CD56+ cells. CD8+ T cells specific for L523S were established in round bottom 96-well plates using 10,000 L523S expressing DCs and 100,000 CD8+ T cells per well in RPMI supplemented with 10% human serum, 10ng/ml of IL-6 and 5ng/ml of IL-12. The cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with L523S, and the costimulatory molecule CD80 in the presence of IL-2. The cells were also stimulated with IFN-gamma to upregulate MHC Class I. The media was supplemented with 10U/ml of IL-2 at the time of stimulation as well as on days 2 and 5 following stimulation. Following three stimulation cycles, ten L523S specific CD8+ T cell lines were identified using interferon-gamma ELISPOT analysis that specifically produce interferon-gamma when stimulated with the L523S tumor antigen-transduced autologous fibroblasts, but not with a control antigen.

One line, 6B1, was cloned using anti-CD3 and feeder cells. The clones were tested for specificity on L523S-transduced fibroblasts. In addition, using a panel of HLA-mismatched lines transduced with a vector expressing L523S and measuring interferon-gamma production by this CTL line in an ELISPOT assay, it was determined that this clone 6B1.4B8 is restricted by HLA-A0201.

Also using transfected Cos cells, it was shown that clone 6B1.4B8 recognizes Cos cells transfected with pcDNA3 HLA A0201/L523S in an HLA-restricted and antigen specific manner.

An epitope mapping study demonstrated the clone 6B1.4B8 recognizes HLA-A201 LCL loaded with peptide pool 3 (a polypeptide corresponding to amino acid positions 33-59 of L523S).

A peptide pool breakdown study demonstrated that clone 6B1.4B8 recognizes autologous B-LCL loaded with 15-mer peptides from amino acid positions 37-55 of L523S, TGYAFVCPDESWALKAIK (SEQ ID NO:465). A further peptide breakdown study demonstrated that clone 6B1.4B8 recognizes T2 cells loaded with the same 15-mer peptides.

A peptide recognition study demonstrated that clone 6B1.4B8 prefers T2 cells loaded with the peptide FVDCPESWAL (SEQ ID NO:466) which corresponds to the amino acid sequence at positions 41-51 of L523S and is encoded by the DNA sequence of SEQ ID NO:467.

EXAMPLE 29

L523S EXPRESSION IN OTHER HUMAN CANCERS

It was previously disclosed in Example 2 that L523S is expressed in lung cancers including squamous, adenocarcinoma and small cell carcinoma. To further evaluate the expression profile of this antigen an electronic expression profiling was performed. This was done by searching a L523S-specific sequence against a public EST database. Results of this profiling indicate that L523S may also be present in colon adenocarcinomas, prostate adenocarcinomas, CML, AML, Burkitt's Lymphoma, brain tumors, retinoblastomas, ovarian tumors, teratocarcinomas, uterus myosarcomas, germ cell tumors as well as pancreatic and cervical tumor cell lines.

EXAMPLE 30

IMMUNOHISTOCHEMISTRY ANALYSIS OF L523S

In order to determine which tissues express the lung tumor antigen L523S, immunohistochemistry (IHC) analysis was performed on a diverse range of tissue types. Polyclonal antibodies specific for L523S (SEQ ID NO:176) were generated as described in Example 23. IHC was performed essentially as described in Example 6. Briefly, tissue samples were fixed in formalin solution for 12-24 hours and embedded in paraffin before being sliced into 8 micron sections. Steam heat induced epitope

retrieval (SHIER) in 0.1 sodium citrate buffer (pH 6.0) was used for optimal staining conditions. Sections were incubated with 10% serum in PBS for 5 minutes. The primary L523S antibody was added to each section for 25 minutes followed by a 25 minute incubation with anti-rabbit biotinylated antibody. Endogenous peroxidase activity was blocked by three 1.5 minute incubations with hydrogen peroxidase. The avidin biotin complex/ horse radish peroxidase (ABC/HRP) system was used along with DAB chromogen to visualize antigen expression. Slides were counterstained with hematoxylin to visualize the cell nuclei.

IHC analysis of L523S expression revealed that of the lung cancer tissues tested over 90% of tissue samples demonstrated high over-expression of the lung tumor antigen (10/11 adenocarcinomas and 8/9 squamous). Of the normal tissues tested, all were negative for expression of L523S, with the exception of weak staining in normal bronchus, testis, liver, and trachea.

EXAMPLE 31

GENERATION AND CHARACTERIZATION OF L762 HUMAN MONOCLONAL

ANTIBODIES

Cell supernatants from hybridoma fusions from the Xenomouse strain of transgenic mice were screened for ability to bind to L762P. All results are shown in Table 13. The primary screen was to test monoclonal supernatants for reactivity to L762P by ELISA analysis using recombinant bacterial expressed protein. We next tested the human supernatants for reactivity to surface expressed L762P by whole cell ELISA using fluorimetry analysis. Specific reactivity of the humab supernatants was confirmed by performing FACS analysis on cells transfected with either an irrelevant plasmid or a plasmid expressing L762P. FI/CFI is the relative fold increase in fluorescence intensity (FI) of the anti-L762P humab primary antibody to irrelevant human primary antibody. FI/CFI/A20 is the relative fold increase in fluorescence intensity (FI) of the anti-L762P humab primary antibody to irrelevant human primary antibody over the FI of the anti-L762P mouse monoclonal antibody 153A20.1. FI/CFI/R690 is the relative fold increase in fluorescence intensity (FI) of the anti-L762P

humab primary antibody to irrelevant human primary antibody over the FI of the anti-L762P rabbit polyclonal antibody. FACS VRL762 is the percentage of cells transfected with plasmid expressing L762P that were positive following staining with indicated monoclonal antibody. FACS VR(-) is the percentage of cells transfected with irrelevant plasmid that were positive following staining with indicated monoclonal antibody. ELISA is the O.D. values of the indicated monoclonal antibody to recombinant L762P protein. The shaded rows in Table 13 indicate those antibodies that will be further cloned and characterized.

Table 13: Human Monoclonal Antibodies Against L762P

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
R-690	4.59		1.00				
M-A20	2.88	1.00					
1.176	0.51	0.18	0.11			0.38	
1.178	1.42	0.49	0.31			0.35	
1.179	0.47	0.16	0.10			0.07	
1.180	1.50	0.52	0.33			0.26	
1.182	1.45	0.50	0.32			0.26	
1.183	0.75	0.26	0.16			0.24	
1.185	0.89	0.31	0.19			0.46	
1.186	3.45	1.20	0.75	32.68	7.14	1.22	1.93
1.187	0.36	0.13	0.08			0.06	
1.188	0.26	0.09	0.06			0.23	
1.189	0.50	0.17	0.11			0.44	
1.190	0.53	0.18	0.12			0.42	
1.191	3.12	1.08	0.68	41.44	17.90	0.86	1.29
1.192	1.91	0.66	0.42			0.12	
1.193	2.87	1.00	0.63	17.82	6.43	0.13	1.06
1.194	1.55	0.54	0.34			0.28	
1.195	0.14	0.05	0.03			0.37	
1.196	1.97	0.68	0.43			0.89	1.64
1.197	0.43	0.15	0.09			0.08	
1.198	0.54	0.19	0.12			0.33	
1.199	0.70	0.24	0.15			0.40	
1.200	2.00	0.69	0.44			0.38	1.56
1.201	1.62	0.56	0.35			0.29	
1.202	0.86	0.30	0.19			0.36	
1.203	1.56	0.27	0.18			0.14	
1.204	3.32	0.58	0.38	24.83	6.60	0.17	1.91
1.205	2.13	0.37	0.25			0.09	
1.206	0.45	0.08	0.05			0.23	
1.207	0.60	0.10	0.07			0.39	
1.208	0.12	0.02	0.01			0.36	
1.209	15.52	2.71	1.80	27.54	9.54	0.16	0.77
1.210	0.92	0.16	0.11			0.16	
1.211	2.83	0.49	0.33			0.42	
1.212	3.40	0.59	0.39	21.68	11.36	0.14	2.47
1.213	2.32	0.40	0.27			0.38	
1.214	0.80	0.14	0.09			0.34	
1.215	3.96	0.69	0.46	38.87	13.17	0.33	1.80
1.216	1.26	0.22	0.15			0.20	
1.217	1.99	0.35	0.23			0.26	

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
1.218	2.29	0.40	0.27			0.10	
1.219	0.15	0.03	0.02			0.06	
1.220	0.82	0.14	0.09			0.21	
1.221	2.29	0.40	0.27			0.12	
1.222	0.57	0.10	0.07			0.45	
1.223	0.11	0.02	0.01			0.11	
1.224	2.08	0.36	0.24			0.25	
1.225	0.95	0.17	0.11			0.22	
1.226	-0.32	-0.06	-0.04			0.06	
R-690	8.62		1.00	72.34	39.83		
M-A20	5.73	1.00		50.23	6.34		
M-A12			67.43	25.15			
M-Irr			7.74	7.35			
R-Irr			30.09	24.80			
H-Irr			25.52	39.14			
R-690	3.20		1.00				
M-A20	2.33	1.00					
1.250	0.15	0.06	0.05			0.28	
1.228	0.38	0.16	0.12			0.08	
1.229	0.39	0.17	0.12			0.44	
1.230	1.78	0.76	0.56			0.13	1.35
1.231	0.42	0.18	0.13			0.47	
1.232	0.34	0.15	0.11			0.25	
1.233	7.07	3.04	2.21	68.84	38.60	0.43	0.75
1.234	2.54	1.09	0.79	33.96	10.94	0.73	1.68
1.235	1.53	0.65	0.48			0.19	1.45
1.236	0.17	0.07	0.05			0.44	
1.237	0.35	0.15	0.11			0.06	
1.238	0.38	0.16	0.12			0.06	
1.239	0.40	0.17	0.13			0.06	
1.240	2.05	0.88	0.64	28.70	7.44	0.33	1.70
1.241	0.41	0.18	0.13			0.41	
1.242	0.52	0.23	0.16			0.05	
1.243	2.34	1.00	0.73	30.94	28.13	0.16	1.33
1.244	0.94	0.40	0.29			0.23	
1.245	0.37	0.16	0.11			0.31	
1.246	2.10	0.90	0.66	13.97	28.92	0.52	1.21
1.247	0.33	0.14	0.10			0.37	
1.248	1.80	0.77	0.56			0.76	
1.249	2.77	1.19	0.86	28.76	12.37	1.15	2.38
1.251	0.22	0.09	0.07			0.47	
1.252	1.16	0.27	0.17			0.37	
1.253	0.07	0.02	0.01			0.43	
1.254	2.05	0.48	0.30			0.14	
1.255	0.09	0.02	0.01			0.08	
1.256	1.17	0.27	0.17			0.13	
1.257	0.42	0.10	0.06			0.06	
1.258	0.48	0.11	0.07			0.40	
1.259	4.82	1.13	0.69	40.24	11.92	0.38	1.78
1.260	1.80	0.42	0.26			0.38	
2.1	2.70	0.63	0.39			0.14	1.35
2.3	0.06	0.01	0.01			0.57	
2.4	3.08	0.72	0.44	31.28	11.43	0.73	1.95
2.5	0.70	0.16	0.10			0.45	
2.6	1.26	0.29	0.18			0.22	
2.8	0.59	0.14	0.09			0.31	
2.9	7.48	1.75	1.08	45.72	17.57	0.95	1.53
2.10	0.35	0.08	0.05			0.42	
2.11	2.71	0.63	0.39			0.60	1.58

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
2.12	6.04	1.41	0.87	52.50	19.59		1.40
2.13	5.50	1.28	0.79	39.78	15.24		1.39
2.14	0.68	0.16	0.10				
2.15	6.51	1.52	0.94	49.90	15.36		1.72
2.16	4.58	1.07	0.66	28.62	13.02		1.51
2.17	8.10	1.89	1.17	48.76	18.24		3.06
R-690	6.94		1.00				
M-A20	4.28	1.00		56.40	5.00		
R-690	4.34	1.65	1.00				
M-A20	2.63	1.00	0.61				
2.18	2.29	0.87	0.53			1.27	1.95
2.20	1.85	0.70	0.43			0.52	2.75
2.21	0.09	0.03	0.02			0.40	
2.22	3.26	1.24	0.75	29.4	6.2	1.45	1.8
2.23	0.31	0.12	0.07			0.12	
2.24	1.21	0.46	0.28			0.65	
2.25	3.47	1.32	0.80	32.5	7.1	1.35	1.46
2.26	4.42	1.68	1.02	35.9	5.5	0.77	1.55
2.27	1.42	0.54	0.33			0.22	
2.28	3.00	1.14	0.69	28.6	5.4	1.21	1.26
2.29	1.41	0.53	0.32			0.58	
2.30	0.42	0.16	0.10			0.43	
2.31	0.09	0.03	0.02			0.07	
2.34	1.94	0.74	0.45			1.17	1.23
2.38	1.14	0.43	0.26			0.09	
2.39	2.50	0.95	0.57	28.2	4.8	0.78	1.14
2.40	2.02	0.77	0.46			0.47	0.99
2.41	1.16	0.44	0.27			0.08	
2.42	0.41	0.16	0.09			0.24	
2.46	2.46	0.93	0.57	16.1	4.6	1.07	1.3
2.47	1.83	0.69	0.42			0.31	1.54
2.48	2.50	0.95	0.58			1.36	1.76
2.49	0.50	0.19	0.12			0.74	
2.50	2.93	1.11	0.68	15.8	4.7	0.52	1.54
2.51	0.13	0.10	0.07			0.30	
2.52	1.11	0.79	0.56	22.1	5	1.14	1.93
2.53	1.87	1.34	0.94	29.8	7.8	0.58	2.84
2.54	1.85	1.32	0.92	15.9	8.5	0.12	2.56
2.55	0.83	0.60	0.42			0.32	
2.58	0.46	0.33	0.23			0.15	
2.60	0.99	0.71	0.50			0.35	
2.61	2.16	1.54	1.08	30.7	7.9	1.34	2.88
2.62	0.36	0.26	0.18			0.58	
2.63	0.37	0.26	0.18			0.41	
2.64	1.60	1.14	0.80	25.7	6.1	1.39	2.85
2.65	0.63	0.45	0.31			0.16	
2.66	0.08	0.06	0.04			0.06	
2.67	1.34	0.96	0.67	23.3	4.5	1.32	1.34
2.68	0.66	0.47	0.33			0.38	
2.69	2.79	1.99	1.39	46.3	9.7	1.47	1.68
2.73	1.47	1.05	0.73	28.5	7.2	1.04	1.85
2.74	1.99	1.43	1.00	39.5	19.1	1.22	1.69
2.75	1.46	1.04	0.73	25.6	7.5	0.68	1.55
2.76	1.61	1.15	0.81	27.7	7.7	0.98	1.79
2.77	1.59	1.13	0.79	27.7	4.9	1.11	1.53
2.78	1.55	1.11	0.77	13.9	8	1.51	2.64
2.79	0.33	0.24	0.16	10	5.4	0.43	
2.80	1.47	1.05	0.73	15.9	8.8	0.46	0.95
R-690	2.00	1.43	1.00				

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
M-A20	1.40	1.00		56.4	5		
R-690	3.76	3.44	1.00				
M-A20	1.09	1.00					
2.81	0.25	0.23	0.07			0.17	
2.82	0.44	0.40	0.12			0.49	
2.83	0.63	0.58	0.17			0.80	
2.84	0.13	0.12	0.04			0.55	
2.85	0.62	0.57	0.16			0.19	
2.86	0.87	0.79	0.23			0.16	
2.87	0.84	0.77	0.22			0.22	
2.89	5.88	5.37	1.56	45.9	37.9	0.07	0.73
2.90	0.23	0.21	0.06			0.60	
2.91	-0.37	-0.34	-0.10			0.43	
2.92	0.59	0.54	0.16			0.14	
2.93	0.28	0.26	0.08			0.44	
2.94	0.32	0.29	0.08			0.46	
2.95	0.39	0.36	0.10			0.51	
2.96	0.36	0.33	0.10			0.26	
2.97	1.26	1.15	0.33	36.8	14.1	1.01	0.89
2.98	0.92	0.84	0.24			0.84	
2.99	1.38	1.26	0.37	91.2	81.8	0.29	
2.100	0.94	0.86	0.25			1.40	
2.102	0.77	0.70	0.21			0.17	
2.104	1.37	1.25	0.36	10.2	7.4	0.14	
2.105	0.63	0.58	0.17			1.04	
2.106	0.79	0.72	0.21			0.84	
2.107	0.81	0.74	0.22			0.06	
2.109	0.66	1.24	0.32	19.2	6.1	0.45	0.89
2.110	1.58	3.00	0.77	36.4	14.2	0.89	1.11
2.112	0.80	1.52	0.39	28.8	6.4	1.16	1.35
2.113	0.57	1.07	0.27	31.4	10.7	0.66	1.17
2.114	0.52	0.99	0.25			0.32	
2.115	1.02	1.94	0.50	19.9	10.7	0.63	1.13
2.116	0.52	0.98	0.25			0.86	
2.118	0.19	0.36	0.09			0.06	
2.119	0.78	1.48	0.38	20.4	5.3	1.22	1.16
2.120	0.76	1.44	0.37	21.8	6	1.29	0.97
2.121	1.24	2.36	0.60	28.7	10.7	0.30	1.17
2.122	1.20	2.29	0.58	31.3	8.3	1.13	1.14
2.123	0.67	1.27	0.33	17.7	6.8	0.74	1.27
R-690	2.06	3.91	1.00				
M-A20	0.53	1.00		56.4	5		
R-690	3.51		1.00				
M-A20	2.91	1.00					
1.1	1.05	0.36	0.30			0.16	
1.2	-0.42	-0.14	-0.12			0.40	
1.3	1.04	0.36	0.30			1.31	
1.4	0.77	0.26	0.22			0.43	
1.5	0.19	0.06	0.05			0.13	
1.6	1.07	0.37	0.30			0.42	
1.7	0.09	0.03	0.03			0.33	0.80
1.8	2.93	1.01	0.83	54.70	45.60	0.59	
1.9	1.17	0.40	0.33			0.93	
1.10	-0.04	-0.02	-0.01			0.08	
1.11	-0.30	-0.10	-0.09			0.16	
1.12	0.11	0.04	0.03			0.25	
1.13	1.60	0.55	0.46			0.08	
1.14	0.69	0.24	0.20			0.13	

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
1.15	0.30	0.10	0.09			0.08	
1.16	1.44	0.49	0.41			0.08	
1.17	-0.31	-0.10	-0.09			0.36	
1.18	0.05	0.02	0.01			0.17	
1.19	-0.34	-0.12	-0.10			0.29	
1.20	0.84	0.29	0.24			0.45	
1.21	-0.20	-0.07	-0.06			0.28	
1.22	0.14	0.05	0.04			0.06	
1.23	0.14	0.05	0.04			0.08	
1.24	1.02	0.35	0.29			0.16	
1.25	0.27	0.28	0.16			0.20	
1.26	1.06	1.09	0.62			0.31	
1.27	1.07	1.10	0.63			0.96	
1.28	2.14	2.21	1.26	3.60	ND	0.06	0.73
1.29	1.11	1.15	0.65			0.44	1.64
1.30	0.79	0.81	0.46			0.19	
1.31	1.42	1.46	0.84			0.23	1.27
1.32	1.37	1.42	0.81			0.11	1.91
1.33	0.29	0.30	0.17			0.18	
1.34	1.59	1.64	0.94	37.53	8.98	1.31	2.61
1.35	0.37	0.38	0.21			0.32	
1.36	0.70	0.72	0.41			0.17	
1.37	1.21	1.24	0.71			0.69	
1.38	0.63	0.65	0.37			0.38	
1.39	0.87	0.90	0.51			0.07	
1.40	0.71	0.73	0.42			0.26	
1.41	1.36	1.40	0.80	43.82	13.65	0.37	2.03
1.42	0.64	0.66	0.38			1.10	
1.43	0.46	0.47	0.27			0.09	
1.44	0.52	0.54	0.31			0.28	
1.45	0.74	0.76	0.44			0.15	
1.46	0.81	0.83	0.48			0.07	
1.47	0.46	0.47	0.27			0.24	
1.48	0.62	0.63	0.36			0.27	
R-690	1.70		1.00				
M-A20	0.97	1.00					
R-690	1.84		1.00				
M-A20	2.82	1.00					
1.49	0.76	0.27	0.41			0.14	
1.50	-0.22	-0.08	-0.12			0.36	
1.51	-0.35	-0.12	-0.19			0.45	
1.52	1.84	0.65	1.00	45.74	9.90	1.40	2.44
1.53	1.77	0.63	0.96	42.79	24.70	0.89	
1.54	1.08	0.38	0.59			0.80	
1.55	0.81	0.29	0.44			0.35	
1.56	1.26	0.45	0.69			0.30	
1.57	3.26	1.16	1.77	22.20	ND	1.31	2.69
1.58	0.81	0.29	0.44			0.80	
1.59	2.22	0.79	1.21	24.50	ND	1.28	2.40
1.60	0.55	0.19	0.30			0.23	
1.61	0.13	0.04	0.07			0.06	
1.62	0.75	0.27	0.41	24.89	10.25	0.12	
1.63	0.99	0.35	0.54			0.25	
1.64	3.60	1.28	1.96			0.06	0.88
1.65	0.32	0.11	0.18			0.29	
1.66	0.01	0.00	0.00			0.30	
1.67	2.00	0.71	1.09	9.30	ND	0.38	
1.68	0.86	0.30	0.47			0.21	
1.69	3.31	1.17	1.80	8.50	ND	0.22	2.39

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
1.70	3.66	1.30	1.99	24.96	12.00	0.84	2.08
1.71	2.01	0.71	1.09			0.21	
1.72	6.49	2.30	3.53	6.50	ND	0.21	1.89
1.73	19.95	0.28	0.21	3.20	ND	0.31	
1.74	19.33	0.27	0.21	5.50	ND	0.20	
1.75	22.25	0.31	0.24			0.10	
1.76	11.42	0.16	0.12			0.37	
1.77	-15.90	-0.23	-0.17			0.08	
1.78	-4.60	-0.07	-0.05			0.26	
1.79	18.78	0.27	0.20			0.25	
1.80	35.51	0.50	0.38	9.00	ND	0.71	
1.81	-4.15	-0.06	-0.04			0.33	
1.82	-37.51	-0.53	-0.40			0.17	
1.83	7.11	0.10	0.08			0.08	
1.84	-21.33	-0.30	-0.23			0.06	
1.85	-3.61	-0.05	-0.04			0.13	
1.86	-19.68	-0.28	-0.21			0.06	
1.87	-3.39	-0.05	-0.04			0.30	
1.88	55.61	0.79	0.59	5.50	ND	0.10	1.25
1.89	-6.73	-0.10	-0.07			0.17	
1.90	11.18	0.16	0.12			0.10	
1.91	-31.50	-0.45	-0.33			0.13	
1.92	-7.56	-0.11	-0.08			0.13	
1.93	-12.37	-0.18	-0.13			0.11	
1.94	49.60	0.70	0.53	14.10	ND	1.39	2.33
1.95	10.68	0.15	0.11			0.16	
1.96	144.63	2.05		63.24	74.75	0.75	0.80
R-690	94.09	1.33	1.00				
M-A20	70.64	1.00					
R-690	7.59		1.00				
M-A20	5.33	1.00					
1.97	1.47	0.28	0.19			0.37	
1.98	3.69	0.69	0.49	38.67	16.57	0.43	1.69
1.99	4.32	0.81	0.57	38.31	18.76	0.40	1.48
1.100	0.22	0.04	0.03			0.32	
1.101	2.06	0.39	0.27			0.49	
1.102	0.23	0.04	0.03			0.12	
1.103	0.33	0.06	0.04			0.28	
1.104	0.45	0.08	0.06			0.08	
1.105	4.19	0.79	0.55	37.19	12.41	0.25	2.18
1.106	4.22	0.79	0.56	46.24	30.59	1.21	1.58
1.107	0.15	0.03	0.02			0.06	
1.108	0.08	0.01	0.01			0.31	
1.109	2.70	0.51	0.36	6.5	6	0.07	
1.110	1.02	0.19	0.13			0.35	
1.111	2.55	0.48	0.34			0.10	
1.112	3.58	0.67	0.47	18.6	4.2	1.25	1.74
1.113	0.37	0.07	0.05			0.35	
1.114	-0.06	-0.01	-0.01			0.27	
1.115	0.55	0.10	0.07			0.13	
1.116	2.24	0.42	0.30			0.44	
1.117	0.56	0.10	0.07			0.27	
1.118	0.77	0.14	0.10			0.43	
1.119	0.78	0.15	0.10			0.41	
1.120	0.73	0.14	0.10			0.58	
1.121	0.21	0.05	0.03			0.40	
1.122	0.11	0.03	0.02			0.29	
1.123	0.41	0.11	0.07			0.07	
1.124	3.66	0.95	0.61	41.27	34.83	0.28	1.85

L762PHumAb	FI/CFI	FI/CFI/A20	FI/CFI/R690	FACSVRL762	FACS VR (-)	ELISA	L762/VR1013
1.125	2.67	0.69	0.44			0.27	1.55
1.126	2.36	0.61	0.39			0.86	1.71
1.127	0.70	0.18	0.12			0.11	
1.128	2.99	0.77	0.50			0.13	1.45
1.129	0.33	0.09	0.06			0.39	
1.130	0.40	0.10	0.07			0.18	
1.131	1.45	0.38	0.24			0.52	
1.132	0.33	0.08	0.05			0.25	
1.133	0.17	0.04	0.03			0.24	
1.134	0.86	0.22	0.14			0.15	
1.135	1.75	0.45	0.29			0.30	
1.136	1.35	0.35	0.23			0.07	
1.137	2.30	0.59	0.38			0.83	1.30
1.138	0.83	0.21	0.14			0.60	
1.139	1.57	0.41	0.26			0.55	
1.140	1.40	0.36	0.23			1.28	
1.142	-0.10	-0.03	-0.02			0.26	
1.143	1.46	0.38	0.24			0.16	
1.144	2.41	0.62	0.40			0.76	
R-690	6.00		1.00				
M-A20	3.86	1.00		56.4	5		
R-690	2.58	3.22	1.00				
M-A20	0.80	1.00					
1.145	0.23	0.29	0.09			0.18	
1.146	-0.12	-0.15	-0.05			0.41	
1.147	0.14	0.18	0.06			0.31	
1.148	0.09	0.11	0.03			0.43	
1.149	0.39	0.49	0.15			0.37	
1.150	2.23	2.79	0.87	17.3	5.4	0.70	1.46
1.151	0.13	0.16	0.05			0.29	
1.152	0.55	0.69	0.21			0.33	
1.154	-0.20	-0.25	-0.08			0.41	
1.155	0.16	0.19	0.06			0.23	
1.156	0.06	0.07	0.02			0.31	
1.158	0.54	0.67	0.21			0.58	
1.159	0.78	0.98	0.30			0.09	
1.160	0.23	0.29	0.09			0.08	
1.162	0.63	0.78	0.24			0.11	
1.163	0.20	0.25	0.08			0.10	
1.164	0.22	0.27	0.08			0.09	
1.166	1.41	1.76	0.55	22.9	5.3	0.52	2.41
1.167	0.32	0.40	0.12			0.08	
1.168	0.88	1.10	0.34	15.9	5.1	0.48	1.90
1.170	0.22	0.42	0.11			0.21	
1.171	0.40	0.76	0.19			0.38	
1.172	0.09	0.17	0.04			0.12	
1.174	0.23	0.43	0.11			0.15	
1.175	0.14	0.26	0.07			0.20	
R-690	2.06	3.91	1.00				
M-A20	0.53	1.00		56.4	5		
for 1.170 to 1.175							
FI-fluorescence intensity of primary antibody							
CFI-fluorescence intensity of human irrelevant primary antibody.							
A20-mouse anti-L762P monoclonal antibody							
R690-rabbit anti-L762P affinity purified polyclonal antibody							
FACS VRL762-percent positive cells from transient transfection of VR1013/L762 expression plasmid							
FACS VR(-)-percent positive cells from transient transfection of empty VR1013 expression plasmid							

EXAMPLE 32

EPITOPE MAPPING AND PURIFICATION OF hL523S-SPECIFIC ANTIBODIES

This Example describes the purification of L523S antibodies that can distinguish between human and mouse L523S homologs and will likely distinguish between hL523S and hL523S-family members such as hIMP-1 and hIMP-2.

L523S (full-length cDNA and amino acid sequence set forth in SEQ ID NO:347 and 348, respectively) is one of a family of proteins that includes hIMP-1 and hIMP-2. The members of this family of proteins have a high degree of similarity one to the other and are also highly similar between species. Thus, generating antibodies that specifically recognize human L523S (hL523S) and not other members of the protein family in humans or the mouse homologs, has been problematic. However, in order to evaluate preclinical and clinical L523S DNA/Adenoviral vaccines by detecting the protein expression of L523S, human L523S-specific antibodies are critical.

Polyclonal antibodies specific for hL523S were generated as described in Example 23. These antibodies were used to map epitopes. The epitope analysis showed 2 particular peptides of hL523S that were recognized, peptide 16/17 and peptide 32.

The amino acid sequences of both hL523S and mouse L523S (mL523S) peptide 16/17 and peptide 32 were then compared. Peptide 32/33 is identical between hL523S and mL523S. However, as the alignment below indicates, peptide 16/17 has 5 amino acid differences between the human and mouse homologs (underlined).

hL523S	(16/17)	(SEQ	ID	NO:468):
I P D E M A A Q Q N P L Q Q P R G R R G L G Q R				
mL523S	(16/17)	(SEQ	ID	NO:469):
I P D E T A A Q Q N P S P Q L R G R R G P G Q R				

Moreover, peptide-based ELISAs showed that peptide 17 is specifically recognized by lung cancer patient sera #197, and a homology search of peptide 17 between human IMP (hIMP) family members shows that there is little similarity in this

region between family members. The hL523S peptide 17 (and 16/17) has less than 50% similarity to hL523S family members such as hIMP-1 and hIMP-2.

Based upon the epitope mapping of L523S-specific antibodies and the data from the homology search, hL523S or mL523S peptide 16/17-conjugated ligands were then used to purify human or mouse L523S-specific antibodies from rabbit polyclonal antibodies generated against hL523S protein as described in Example 23. The data from the antibodies purified by affinity chromatography using ligands conjugated with either hL523S-peptide 16/17 or mL523S-peptide 16/17 suggested that the affinity of antibodies specific to hL523S-peptide 16/17 is much higher than that of antibodies to mL523S-peptide 16/17 since they bind more strongly to hL523S-peptide 16/17 than to mL523S-peptide 16/17. The difference in affinity between the purified antibodies to human and mouse L523S-peptide 16/17 was confirmed by peptide-based ELISA. The antibodies purified by hL523S-peptide 16/17 selectively bind to human L523S-peptide 16/17 but bind much less or not at all to mL523S-peptide 16/17.

In order to further characterize the original polyclonal antibodies and antibodies purified by hL523S-peptide 16/17, immunoblot analysis was conducted using both human lung adenocarcinoma line as a source of hL523S protein and mouse whole body embryo (day 17 gestation) as the source of mL523S protein. This analysis showed that polyclonal antibodies specific for hL523S recognize hL523S protein expressed in the tumor cell line as well as mL523S protein expressed in whole body embryos of day 17 gestation. However, the addition of hL523S peptide 32/33 blocks binding of antibodies to human and mouse L523S proteins. Thus, the crossreactivity of the polyclonal antibodies to mL523S protein is due to the existence of antibodies specific to hL523S peptide 32/33. In marked contrast, the purified antibodies specific to hL523S peptide 16/17 do not bind mL523S protein expressed in mice embryos but do recognize hL523S protein expressed in human lung adenocarcinoma cells. These data confirm the ELISA data using hL523S-peptide 16/17 and mL523S-peptide 16/17 described above.

The amino acid sequence of hL523S peptide 16/17 used to purify the antibodies is about 60-70% similar to that of the mL523S-peptide 16/17 which is not recognized by hL523S-specific antibodies by Western blot analysis and peptide-based ELISA. The hL523S peptide 16/17 has less than 50% similarity to hL523S family

members such as hIMP-1 and hIMP-2. Taken together, these data suggest that it is highly probable that the antibodies purified by hL523S peptide 16/17 described herein will also distinguish hL523S protein from the other hL523S family members.

In summary, antibodies purified with the hL523S peptide 16/17 do not recognize the mouse L523S homolog. The amino acid sequence of peptide 16/17 between hL523S family members is less similar than between human and mouse L523S. Thus, the hL523S-specific antibodies described above can be used to distinguish between human and mouse L523S and between members of the hL523S family of proteins and can therefore be used for the accurate detection of hL523S protein expression in animals and humans.

EXAMPLE 33

IN VIVO IMMUNOGENECITY OF LUNG TUMOR ANTIGEN L523

This example describes two *in vivo* immunogenicity studies to evaluate the vaccination of mice with either an adenovirus containing L523 or with L523 naked DNA followed by a second immunization with an adenovirus containing L523.

The first study involved the immunization of two strains of mice with L523 adenovirus. The C57BL6 strain of mice is homozygous for HLA-type H-2^b, while strain B6D2(F1) is heterozygous for the HLA-type, H-2^{b/d}. Table 14 describes the initial immunization strategy employed.

Table 14: Immunization with L523 Adenovirus alone: Experimental Design

Group	Immunization	Strain (4/group)
1	10 ⁸ PFU Ad L523 A	C57BL6
2	10 ⁷ PFU Ad hrGFP A	C57BL6
3	10 ⁸ PFU Ad L523 A	B6D2(F1)
4	10 ⁷ PFU Ad hrGFP A	B6D2(F1)
5	Naïve	C57BL6
6	Naïve	B6D2(F1)

PFU=plaque forming unit; GFP=green fluorescent protein; Ad=adenovirus.

Mice were immunized intradermally with either 10^8 PFU of L523-adenovirus or 10^7 PFU of an irrelevant adenovirus (hrGFP). Three weeks following immunization, IgG1 and IgG2a antibody responses to L523 were examined in all groups of mice. Briefly, recombinant full length L523 (rL523) was coated onto ELISA plates and serum, at multiple dilutions, was added to the wells. Following a 60-minute incubation, the serum was washed from the wells and a secondary antibody, either specific for an IgG1 or IgG2a was added to the plates. Both antibodies were directly conjugated to horseradish peroxidase (HRP). The levels of L523 antibodies, either IgG1 or IgG2a, were measured in all groups. In the C57BL6 mice, little to no L523-specific antibodies were detected following immunization. However, in the B6D2(F1) strain of mice immunized with L523 adenovirus, both IgG1 and IgG2a L523-specific antibodies were detected at serum dilution as low as 1/1000.

In addition to detecting L523-specific antibodies in the serum, interferon-gamma (IFN- γ) responses were assayed from immune spleen cells following *in vitro* stimulation with rL523 protein. Briefly, spleen cells were harvested from all mice groups and cultured for 3 days in 96-well plates. Culture conditions included, media alone, 1 or 10 μ g/ml of rL523 protein, or 5 μ g/ml of concanavalin A (Con A). After 3 days, the supernatants were harvested and assayed for IFN- γ levels in the supernatants.

Immunization with L523-adenovirus, but not an irrelevant adenovirus, elicited a strong IFN- γ response from the spleen cells which were stimulated with rL523. In general, responses were stronger in the B6D2(F1) mouse strain, as evidenced by both a higher level of IFN- γ production, as well as the fact that stimulation with a lower antigen concentration (1 μ g/ml) elicited an equally strong response as seen with the higher antigen concentration (10 μ g/ml).

Finally, T cell proliferation responses were assayed from immune spleen cells by stimulation *in vitro* with rL523 protein. Briefly, spleen cells were cultured for 4 days in 96-well plates with, media alone, 1 or 10 μ g/ml of rL523 protein, or Con A. The cultures were then pulsed with 3H-thymidine for the final 8 hours of culture. Results are represented as the stimulation index (SI) in the presence of antigen relative to stimulation with media alone. Results were consistent with those obtained in the IFN- γ

assay. Immunization with L523-adenovirus, but not an irrelevant adenovirus, elicited a proliferation response in spleen cells stimulated with rL523. A strong SI (average of >20) was observed in spleen cells harvested from the B6D2(F1) mouse strain, with similar levels of proliferation observed at both protein concentrations. Little or no T cell proliferation was observed in the C57BL6 mouse strain.

A second study involved the immunization of two strains of mice initially with L523 naked DNA followed by a second immunization with L523 adenovirus two weeks later. The mice were harvested 3 weeks after the boost. Table 15 describes the immunization regimen of the second study.

Table 15: Immunization with L523 DNA followed by a second immunization with L523-Adenovirus; Experimental Design

Group	Immunization	Strain (4/group)
1	L523 DNA + 10^8 PFU Ad L523 A	C57BL6
2	10^8 PFU Ad L523 A	C57BL6
3	Irrelevant DNA + 10^7 PFU Ad hrGFP A	C57BL6
4	10^7 PFU Ad hrGFP A	C57BL6
5	Naïve	C57BL6
6	L523 DNA + 10^8 PFU Ad L523 A	B6D2(F1)
7	10^8 PFU Ad L523 A	B6D2(F1)
8	Irrelevant DNA + 10^7 PFU Ad hrGFP A	B6D2(F1)
9	10^7 PFU Ad hrGFP A	B6D2(F1)
10	Naïve	B6D2(F1)

PFU=plaque forming unit; GFP=green fluorescent protein; Ad=adenovirus.

As described in the first study, strong IgG1 and IgG2a antibody responses were observed in B6D2(F1) mice following immunization with L523-adenovirus. Immunizing with L523 DNA appeared to increase the overall L523-specific antibody response compared to responses achieved with immunization with L523-adenovirus alone. C57BL6 mice elicited little or no L523-specific antibody responses following immunization with L523-adenovirus, but were some slightly positive responses were detected in mice immunized with L523 DNA followed by a second immunization with L523-adenovirus.

IFN- γ responses were assayed from immune spleen cells by stimulation *in vitro* with rL523 protein. These results confirm those observed in the initial study demonstrating the immunogenicity of L523 in animals. The results also suggest that initially immunizing the animals with L523 DNA, prior to immunization with L523-adenovirus, does not significantly increase the CD4 response. As with the initial study, responses appear to be stronger in the B6D2(F1) strain of mice than the C57BL6 strain.

As with the initial study, T cell proliferation responses were assayed from immune spleen cells by stimulation *in vitro* with rL523 protein. The results from using two rounds of immunization are consistent with those obtained from the first study. Immunization with L523 DNA prior to a second round of immunization with L523-adenovirus did not significantly increase the proliferation responses generated in the mice. As with the first study, responses were stronger in the B6D2(F1) mouse strain than in the C57BL6 strain.

The difference in HLA types between the two strains of mice could explain variations in the extent of the immune responses detected. As described above, the C57BL6 strain is homozygous for H-2^b, while the B6D2(F1) is heterozygous for H-2^{b/d}. The increased diversity of the B6D2(F1) strains HLA type allows for a greater number of epitopes derived from the L523 protein to be presented. In this strain, epitopes specific for both H-2^b and H-2^d can be presented, while only H-2^b epitopes can be presented by the C57BL6 strain.

From the foregoing it will be appreciated that, although specific embodiments of the invention have been described herein for purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the invention is not limited except as by the appended claims.

CLAIMS

What is Claimed:

1. A method for inducing an immune response in an animal, comprising:
 - a) providing a composition comprising a polynucleotide encoding at least an immunogenic portion of a lung carcinoma polynucleotide wherein the polynucleotide has at least 90% identity with SEQ ID NO:347;
 - b) administering said polynucleotide; and
 - c) thereby inducing an immune response in an animal.
2. The method of claim 1, wherein said composition further comprises a component selected from the group consisting of a physiologically acceptable carrier or an adjuvant.
3. A method according to claim 1, wherein the lung carcinoma polynucleotide is delivered by a viral based delivery system.
4. A method according to claim 3, wherein the viral based delivery system is an adenovirus.
5. The method of claim 1, wherein the immune response induced is a CD4+ T helper response.
6. The method of claim 1, wherein the immune response induced is a CD8+ cytotoxic T lymphocyte response.
7. The method of claim 1, wherein the immune response induced is both a CD4+ T helper and CD8+ cytotoxic T cell immune response.

8. An isolated polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences provided in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;

(b) complements of the sequences provided in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;

(c) sequences consisting of at least 10 contiguous residues of a sequence provided in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;

(d) sequences that hybridize to a sequence provided in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467, under highly stringent conditions;

(e) sequences having at least 75% identity to a sequence of SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467;

(f) sequences having at least 90% identity to a sequence of SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467; and

(g) degenerate variants of a sequence provided in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467.

9. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

(a) sequences having at least 90% identity to a polypeptide having an amino acid sequence of any one of the sequences provided in SEQ ID NO:352, 354, 357, 361, 363, 365, 367, 369, 376-382, 387-419, 423, 427, 430, 433, 441, 443, 446, 449, 451-466 and 468-469;

(b) sequences encoded by a polynucleotide of claim 8;

(c) sequences having at least 70% identity to a sequence encoded by a polynucleotide of claim 8; and

(d) sequences having at least 90% identity to a sequence encoded by a polynucleotide of claim 8.

10. An expression vector comprising a polynucleotide of claim 8 operably linked to an expression control sequence.

11. A host cell transformed or transfected with an expression vector according to claim 10.

12. An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a polypeptide of claim 9.

13. A method for detecting the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with a binding agent that binds to a polypeptide of claim 9;
- (c) detecting in the sample an amount of polypeptide that binds to the binding agent; and
- (d) comparing the amount of polypeptide to a predetermined cut-off value and therefrom determining the presence of a cancer in the patient.

14. A fusion protein comprising at least one polypeptide according to claim 9.

15. A fusion protein according to claim 14, wherein the fusion protein is selected from the group consisting sequences provided in SEQ ID NO:352, 354, 423, 427, 430 and 433.

16. An oligonucleotide that hybridizes to a sequence recited in SEQ ID NO:351, 353, 358, 362, 364, 366, 368, 370-375, 420, 424, 428, 431, 434, 442, 447, 450 and 467 under highly stringent conditions.

17. A method for stimulating and/or expanding T cells specific for a tumor protein, comprising contacting T cells with at least one component selected from the group consisting of:

- (a) polypeptides according to claim 9;
- (b) polynucleotides according to claim 8; and
- (c) antigen-presenting cells that express a polynucleotide according to claim 8,

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

18. An isolated T cell population, comprising T cells prepared according to the method of claim 17.

19. A composition comprising a first component selected from the group consisting of physiologically acceptable carriers and immunostimulants, and a second component selected from the group consisting of:

- (a) polypeptides according to claim 9;
- (b) polynucleotides according to claim 8;
- (c) antibodies according to claim 12;
- (d) fusion proteins according to claim 14;
- (e) T cell populations according to claim 18; and
- (f) antigen presenting cells that express a polypeptide according to claim 9.

20. A method for stimulating an immune response in a patient, comprising administering to the patient a composition of claim 19.

21. A method for the treatment of a lung cancer in a patient, comprising administering to the patient a composition of claim 19.

22. A method for determining the presence of a cancer in a patient, comprising the steps of:

- (a) obtaining a biological sample from the patient;
- (b) contacting the biological sample with an oligonucleotide according to claim 9;
- (c) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and
- (d) compare the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence of the cancer in the patient.

23. A diagnostic kit comprising at least one oligonucleotide according to claim 16.

24. A diagnostic kit comprising at least one antibody according to claim 12 and a detection reagent, wherein the detection reagent comprises a reporter group.

25. A method for the treatment of lung cancer in a patient, comprising the steps of:

- (a) incubating CD4+ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of: (i) polypeptides according to claim 9; (ii) polynucleotides according to claim 8; and (iii) antigen presenting cells that express a polypeptide of claim 9, such that T cell proliferate;
 - (b) administering to the patient an effective amount of the proliferated T cells,
- and thereby inhibiting the development of a cancer in the patient.

SEQUENCE LISTING

<110> Corixa Corporation
 Wang, Tongtong
 Wang, Aijun
 Skeiky, Yasir A.W.
 Li, Samuel X.
 Kalos, Michael D.
 Henderson, Robert A.
 McNeill, Patricia D.
 Fanger, Neil
 Retter, Marc W.
 Durham, Margarita
 Fanger, Gary R.
 Vedvick, Thomas S.
 Carter, Darrick
 Watanabe, Yoshihiro
 Peckman, David W.
 Cai, Feng
 Foy, Teresa M.

<120> COMPOSITIONS AND METHODS FOR THE THERAPY
 AND DIAGNOSIS OF LUNG CANCER

<130> 210121.45503PC

<140> PCT

<141> 2001-11-30

<160> 469

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 315

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 236, 241

<223> n = A,T,C or G

<400> 1

```
gcagagacag actggtgggt gaacctggag gtgccaaaa agccagctgc gggcccagga 60
cagctgcgcg gagactcccg atgtcacagg cagtctgtgt ggttacagcg cccctcagtg 120
ttcatctcca gcagagacaa cggaggaggc tccccaccag acggttctca ttatttatat 180
gttaatatgt ttgtaaactc atgtacagtt ttttttgggg gggaagcaat gggaanggta 240
naaattacaa atagaatcat ttgctgtaat ccttaaatgg caaacggtca ggccacgtga 300
aaaaaaaaaa aaaaaa                                     315
```

<210> 2

<211> 380

<212> DNA

<213> Homo sapiens

<400> 2

```
atttaggctt aagatcttgt ttacccttgt tactaaggag caaattagta ttaaagtata 60
atatatatata acaaatataca aaagtcttga gtggttcagc ttttttattt tttttaatgg 120
cataactcttt aacaacactg ctctgtaalg ggttgaactg tgggtactcag actgagataa 180
ctgaaatgag tggatgtata gtgttatigc ataattatcc cactatgaag caaagggact 240
ggataaattc ccagctctaga ttattagcct ttgttaacca tcaagcacct agaagaagaa 300
ttattggaaa ttttgcctc tgtaactggc accttgggggt gtgacttacc ttttgccttt 360
gtaaaaaaa aaaaaaaaaa 380
```

<210> 3

<211> 346

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 316, 317, 318, 322, 323, 326, 329, 330, 331, 336, 337, 339,
340, 342, 343

<223> n = A,T,C or G

<400> 3

```
ttgtaagtat acaatttttag aaaggattaa atgtttattga tcattttact gaatactgca 60
catctccacc atacaccatc cactttccaa taacatttaa tcctttctca aattgtaagt 120
atacaattgt actttctttg gattttcata acaaatatac catagactgt taattttatt 180
gaagtcttct taatggaatg agtcatcttt gtctgtgtgt tttgagggtta ccttgccttt 240
gacttccaac aatttgatca tatagtgttg agctgtggaa atctttaaagt ttattctata 300
gcaataattt ctattnnag annccngggn naaaannann annaaa 346
```

<210> 4

<211> 372

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 297, 306, 332

<223> n = A,T,C or G

<400> 4

```
actagtctca ttactccaga attatgctct tgtacctgtg tggctggggt tcttagtcgt 60
tggtttgggt tggttttttg aactgggtat taggggtgggt cacagtctca atgtaagcac 120
tctcttctcc aagtgtgtct ttgtggggac aatcattctt tgaacattag agagggaaggc 180
agtccaagct gttgaaaaga ctattgcctta tttttgtttt taaagacctt cttgacgtca 240
tgtgacagct gcacgtgcct tacgctacat cttgttttct aggaagaagg ggatgcnggg 300
aaggantggg tgctttgtga tggataaaac gnotaaaata cacaccttta cattttgaaa 360
aaaaaazaac aa 372
```

<210> 5

<211> 698

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 8, 345, 422, 430, 433, 436, 438, 472, 481, 486, 515, 521,
536, 549, 553, 556, 557, 559, 568, 593, 597, 605, 611, 613,

616, 618, 620, 628, 630, 632, 634, 635, 639, 643, 647, 648,
649, 652, 654, 658, 664, 690
<223> n = A,T,C or G

<400> 5
actagtanga tagaaacact gtgtcccgag agtaaggaga gaagctacta ttgattagag 60
cctaaccagc gtttaactgca agaagaggcg ggatactttc agctttccat gtaactgtat 120
gcataaagcc aatgtagtcc agttttctaag atcatgtttc aagctaactg aatcccaatt 180
caatacacac tcagtgaact ctgatggaac aataacaggc ccaagcctgt ggtatgatgt 240
gcacacttgc tagactcaga aaaaatacta ctctcataaa tgggtgggag tattttgggt 300
gacaacctac tttgcttggc tgagtgaagg aatgatatto atatnttcat ttattccatg 360
gacatttagt tagtgctttt tatataccag gcgatgtgct gagtgacact ctgtgtgata 420
tntccaaatn ttngtncngt cgctgcacat atctgaaatc ctatattaag antttcccaa 480
natgangtcc ctggtttttc caccgccatt gatcngtcaa ngatctaac tctgtntgtc 540
ctaaaaccnt ctctnnnang gttagacngg acctctcttc tcccttcccg aanaatnaag 600
tgtgngaaga nanccnncn cccctctnnc tcnncctnng ccnctnnnc cncatgtngg 660
ggngccgccc ccccgggggg gacccccccc ttttcccc 698

<210> 6
<211> 740
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 82, 406, 426, 434, 462, 536, 551, 558, 563, 567, 582, 584,
592, 638, 651, 660, 664, 673, 675, 697, 706, 711, 715, 716,
717, 723, 724, 725, 733
<223> n = A,T,C or G

<400> 6
actagtcaaa aatgctaaaa taatttggga gaaaatattt ttaagttagt gttatagttt 60
catgttttat ttttattatg tnttgtgaag ttgtgtcttt tcactaatta cctatactat 120
gccaatattt ccttatatct atccataaca tttatactac atttgaaga gaatatgcac 180
gtgaaactta acactttata aggtaaaaat gaggtttcca agatttaata atctgatcaa 240
gttcttgtta tttccaaata gaatggactt ggtctgttaa ggggctaagg gagaagaaga 300
agataaggtt aaaagtgtgt aatgacccaa cattctaaaa gaaatgcгаа aaaaaattta 360
ttttcaagcc ttcgaaactat ttaaggaaag caaaatcatt tcctanatgc atatcatttg 420
tgagantttc tcantaatat cctgaatcat tcatcttcagc tnaggcttca tgttgactgc 480
atatgtcatc tagggaaagt ctatttcacg gtccaaacct gttgccaatg ttggtnaggc 540
tttcttttaa ntgtgaanta ttnacangaa attttctctt tnanagttct tnataggggt 600
aggggtgtgg gaaaagcttc taacaactctg taggtgttncg gtttatctgt ncagaaccan 660
aatnacggat cgnangaagg actgggtcta tttacangaa cgaatnatct ngttnnntgt 720
gtnnncaact ccngggagcc 740

<210> 7
<211> 670
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 265, 268, 457, 470, 485, 546, 553, 566, 590, 596, 613, 624,
639, 653, 659, 661
<223> n = A,T,C or G

<400> 7
gctggggagc tcggcatggc ggtccccgct gcagccatgg ggcctcggc gttggggcag 60

```

agcgggccccc gctcgatggc cccgtgggtgc tcagtgagca gcgggcccgtc ggcgtacgtg 120
cttgggatgc aggaactgtt ccggggccac agcaagaccg cgagttcctg gcgcacagcg 180
ccaaggtgca ctcggtggcc tggagtttgc acgggctcg cctacotcgg ggtcttcgac 240
aagacgccac gtcttcttgc tgganaanga ccgttgggtca aagaaaacaa ttatcgggga 300
catggggata gtgtggacca ctttgttggc atccaagtaa tcctgacota tttgttacgg 360
cgtctggaga taaaaccatt cgcactctgg atgtgaggac taaaaatgc attgccactg 420
tgaacaactaa aggggagaac attaatatct gctggantcc tgatgggcan accattgtcg 480
tagcnacaag gatgatgtgg tgacttttatt gatgccaa gaaccccgctc caaagcaaaa 540
aaacanttcc aanttcgaag tcaccnaaat cctctgggaa aatgaacatn aatatnttct 600
tcctgacaaat gncncttggg tgnntoacat cctcagctnc cccaaaactg aanctgttnc 660
natccacccc

```

```

<210> 8
<211> 689
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 253, 335, 410, 428, 448, 458, 466, 479, 480, 482, 483, 485,
488, 491, 492, 495, 499, 500, 502, 503, 512, 516, 524, 525,
526, 527, 530, 540, 546, 550, 581, 593, 594, 601, 606, 609,
610, 620, 621, 622, 628, 641, 646, 656, 673
<223> n = A,T,C or G

```

```

<400> 8
actagtatct aggaatgaac agtaaaagag gacgagttgg ctacttgatt acaacagagt 60
aaatgaagta ctggatttgg gaaaacctgg ttttattaga acatatggaa tgaagaccta 120
caoctagcat tgcctaacta gccccctgaa ttaacagagc ccaattgaga caaacccctg 180
gcaacaggaa attcaaggga gaaaagtaa gcaacttggg ctaggatgag ctgactccct 240
tagagcaaaag ganagacagc cccattacc aaataccatt ttggcctggg gcttgtgcag 300
ctggcagatgt tcttgcacca gcatggcacc ttatngtttt gatagcaact tcttgaatt 360
ttcacaacta tattaactga aattataata tagcctgtcc gtttgcctgn tccaggctgt 420
gatataatnt cctagtgggt tgacttttaa aataaatnag gttantttt ctcccccn 480
cnntnctncc nntnctnccn cnntcccccc cncctngtcc tcnnnnttn gggggggccn 540
cccccnccgn ggacccccct ttggtccctt agtggaggtt natggccctc ggnnttatcc 600
nggcctannn ttccccgtn nnaaatgntt cccctccca ntcnccncc ccaanccgg 660
aagcctaagt ttntaccctg ggggtcccc

```

```

<210> 9
<211> 674
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 602, 632, 639, 668
<223> n = A,T,C or G

```

```

<400> 9
gtccactctc ctttgagtgt actgtcttac tgtgcactct gtttttcaac ttcttagata 60
taaaaaatgc ttgttctata gtggagtaag agctcaacac ccaaggcgag caagataact 120
gaaaaaagcg aggccttttt gccaccttgg taaaggccag ttcactgtcta tagaactgct 180
ataagcctga aggggaagtag ctatgagact ttccattttt cttagttctc ccaataggct 240
ccttcatgga aaaaggcttc ctgtaataat ttccacctaa tgaattagca gtgtgattat 300
ttctgaaata agagacaat tgggcgcagc agtcttctcg tgatttaaaa taaacaaccc 360
aaagtittgt ttgttctcca ccaaggaca tactctaggg ggtatgtgtg tgaagacatt 420
caaaaacatt agctgttctg tctttcaatt tcaagttatt ttggagactg cctccatgtg 480

```

```

agttaattac tttgctctgg aactagcatt attgtcatta tcatcacatt ctgtcatcat 540
cacttgaata atattgtgga ttccccctc tgcttgcata ttcttttgac tcctctggga 600
anaaatgtca aaaaaaaagg tcgatctact cngcaagnc catctaata ctgcgctgga 660
aggaccnct gcc 674

```

```

<210> 10
<211> 346
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 320, 321, 322, 325, 326, 328, 329, 330, 332, 333, 334, 335,
342
<223> n = A,T,C or G

```

```

<400> 10
actagtctgc tgaatgaaag cactatacat cctattgttt cttcttttc aaaaatcagcc 60
ttctgtctgt aaaaaaatg tactttatag agatggagga aaaggtctaa tactacatag 120
ccttaagtgt ttctgtcatt gttcaagtgt attttctgta acagaaacat attttggaatg 180
ttttcttttt cccctataaa attgtaattc ctgaaatact gctgotttaa aaagtccac 240
tgtcagatta tattatctaa caattgaata ttgtaaatat acttgttcta cctctcaata 300
aaagggtact tttctattan nnagngnnnn gnnnnataaa aaaaaa 346

```

```

<210> 11
<211> 602
<212> DNA
<213> Homo sapiens

```

```

<400> 11
actagtaaaa agcagcattg ccaataaatc cctaattttc cactaaaaat ataataaat 60
gatgttaagc tttttgaaaa gtttagggtta aacctactgt tgtaggatta atgtatttgt 120
tgcttccctt tatctggaat gtggcattag cttttttatt ttaacctctt ttaattctta 180
ttcaattcca tgacttaagg ttggagagct aaacactggg atttttgat aacagactga 240
cagttttgca taattataat cggcattgta catgaaaagg atatggctac cttttgttaa 300
atctgcactt tctaaatato aaaaaaggga aatgaagtta taaatcaatt ttgttataat 360
ctgtttgaaa catgagtttt atttgcttaa tattaggcct ttgccccctt tctgtaagt 420
tcttgggato ctgtgtagaa ctgttctcat taaacaccaa acagttaagt ccattctctg 480
gtactagcta caaattcggt ttcatattct acttaacaat ttaataaac tgaatatatt 540
ctagatggct tactttctgt catataaaaa caaaacttga ttccaaaaa aaaaaaaa 602
aa

```

```

<210> 12
<211> 685
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 170, 279, 318, 321, 322, 422, 450, 453, 459, 467, 468, 470,
473, 475, 482, 485, 486, 491, 498, 503, 506, 509, 522, 526,
527, 528, 538, 542, 544, 551, 567, 568, 569, 574, 576, 582,
587, 588, 589, 590, 592, 593, 598, 599, 603, 605, 608
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 633, 634, 635, 644, 646, 648, 651, 655, 660, 662, 663, 672,
674, 675, 682, 683

```


<223> n = A,T,C or G

<400> 12

```
actagtccgtg tgaagtacac actgaaggca gaaagtgtta ggtattttgca tctaattgttc 60
attatcatcgtg tattgatgga cctaagaaaa taaaatttag actaagcccc caaataagct 120
gcatgcatttt gtaacatgat tagtagatttt gaatatatag atgtagatn ttgggtatct 180
agggtttttta tcattatgta aaggaattaa agtaaaaggac ttgttagttg tttttattaa 240
atatgcabat agtagagtgcc aaaaatatag caaaaatana aactaaagggt agaaaagcat 300
tttagatatg ccttaainta nnaactgtgc caggtggccc tcggaataga tgccaggcag 360
agaccagtgc ctgggtgggt cctcccccctg tctgcccccc tgaagaactt cctccacgtg 420
angtagtgcc ctgtagtggt tcacgtggan tantggganc aggcggnnncn gtnanaagaa 480
ancannnngt nagtttcncc gtngangcng aactgtccct gngcnnnnac gctcccaaaa 540
cntntccaat ngacaatcga gtttccnnnc tcnagnaacc tngcggnnnn cnggccnncc 600
cantntgnta accccgcgcc cggatcgctc tcnnntcgtt ctcnncncaa ngggntttcn 660
cnncgcgcgt cncnnccccc cnncc 685
```

<210> 13

<211> 694

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 503, 546, 599, 611, 636, 641, 643, 645, 656, 658, 662, 676, 679, 687

<223> n = A,T,C or G

<400> 13

```
cactagtccac tcattagcgt ttccaatagg gctcttaagt ccagtagatt acgggtagtc 60
agttgacgaa gatctggttt acaagaacta attaaatggt tcattgcatt ttgtgaagaa 120
cagaataatt ttataaaatg ttgttagttt ataattccgc aaaataaatt aaagacactt 180
tttctctgtg tgtgcaaatg ttgtttttgt atccattttt tttttttttt taggacacct 240
gtttactagc tagctttaca atatgccaaa aaaggatttc tccctgacct catcogtgg 300
tcaccctctt ttcccccat gctttttgcc ctagtattata acaagggaat gatgatgatt 360
taaaaagtag ttctgtatct tcagtatctt ggtcttccag aaccctctgg ttgggaagg 420
gatcattttt tactggtcat ttccctttgg agtgtaactc tttaacagat ggaaagaact 480
cattggccat ggaaacagcc gangtggttg gagccagcag tgcattggcac cgtccggcat 540
ctggcctgat tggctcggct gccgtcattg tcagcacagt gccatgggac atgggggaana 600
ctgactgcac ngccaatggt ttcatgaag aatacngcat ncnngtcat cacytnanco 660
angacgctat ggggngcana gggccanttg ctcc 684
```

<210> 14

<211> 679

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 29, 68, 83, 87, 94, 104, 117, 142, 145, 151, 187, 201, 211, 226, 229, 239, 241, 245, 252, 255, 259, 303, 309, 359, 387, 400, 441, 446, 461, 492, 504, 505, 512, 525, 527, 533, 574, 592, 609, 610, 618, 620, 626, 627, 633, 639, 645, 654

<223> n = A,T,C or G

<400> 14

```
cagccgcctg catctgtatc cagcgccang tccgccagat cccagctgcy cgcgcccccc 60
agtcgccnac ccgttcggcc cangctnagt tagncctcac catnccgctc aaaggngaca 120
ccaagtgcac caaatccctg cngtncggat ntaaatctcat ctctcggctt gccgggatg 180
```

```

ctgtccntgc cattggacta nggctccgat ncgactctca gaccanganc atcttcganc 240
naganaactaa tnatnatnt tccagcttct acacaggagt ctatattctg atccggtccg 300
gncnccctent gatgctgtgt ggcttctctga gctgctgcgg ggctgtgcaa gagtcccant 360
gcagtctggg actgttcttc ggcttctctt tgggtgattn cgccattgaa atacctgcgg 420
ccatctgggg atattccact ncgatnatgt gattaaggaa ntccaaggag ttttacaagg 480
acacgtacaaa cnacctgaaa accnnggatg anccccaccg ggaancnctg aangccatcc 540
actatgcggt gaactgcaat ggtttggctg ggnccttga acaatttaac cnatatacat 600
tgggcccaann aaaggacntn ctcganncct tcnccgtgna attcngttct gatnccatca 660
cagaagtctc gaacaatcc

```

```

<210> 15
<211> 695
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 105, 172, 176, 179, 189, 203, 212, 219, 221, 229, 231, 238,
242, 261, 266, 270, 278, 285, 286, 298, 311, 324, 337, 350,
363, 384, 391, 395, 405, 411, 424, 427, 443, 448, 453, 455,
458, 463, 467, 470, 479, 482, 484, 493, 499, 505, 518
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 520, 523, 531, 540, 584, 595, 597, 609, 611, 626, 628, 651,
652, 657, 661, 665, 669, 672, 681, 683, 691, 693
<223> n = A,T,C or G

```

```

<400> 15
actagtggat aaaggccagg gatgctgctc aacctctctac catgtacagg gacgtctccc 60
cattacaact acccaatccg aagtgtcaac tgtgtcagga ctaanaaacc ctggttttga 120
ttaaaaaagg gcttgaaaaa aggggagcca caaatctgtc tgcttctctca cnttantent 180
tggcaaatna gcatcttgtc tcnttggctg cngcctcanc ncaaaaaanc ngaactcnat 240
cngggccagg aatacatctc ncaatnaacn aaattganca aggcnnntgg aaatgccnga 300
tgggattatc ntccgcttgt tgancttcta agtttctntc ccttcatton accctgccag 360
cnnagttctg ttagaaaaat gcngaattc naacncoggt tttctactc ngaattttaga 420
tctncanaaa ctctctggcc acnaticnaa ttanangnca cgnacanatn ccttccatna 480
anncncccc acmtttgana gccangacaa tgactgcmtn aantgaaggc ntgaaggaaan 540
aactttgaaa ggaaaaaaa ctttgtttcc ggccccctcc aacncttctg tgttnanac 600
tgccctctng naaccttga agcccnnga cagtgttaca tgttgtteta nnaaacngac 660
nctnaatnt cnatcttccc nanaacgatt ncncc

```

```

<210> 16
<211> 669
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 299, 354, 483, 555, 571, 573, 577, 642, 651, 662, 667
<223> n = A,T,C or G

```

```

<400> 16
cgccgaagca gcagcgagg ttgtcccggt tttccctccc ctttcccttc tccggttgcc 60
ttccggggcc cttacactc cacagtcccg gtcccggcat gtcccagaaa caagaagaag 120
agaacctctg ggaggagacc ggcgaggaga agcaggacac gcaggagaaa gaaggtatcc 180
tgccgtgagag agctgaagag gcaaaagctaa agggcaataa ccaagccta ccaagccta 240
ctggaggctc cgacttcttc atgaagagac tccagaaagg gcaaaagatc ttgactcng 300

```

```

gagactacaa catggccaaa gccaacatga agaataagca gctgccaaagt gcangaccag 360
acaagaacct ggtgactggt gatcacatcc ccaccccaca ggatctgccc agagaaagtc 420
ctgctctctc accagcaagc ttgctgggtgg ccaagttgaa tgatgtctgcc ggggctctgc 480
canatctgag acgcttccct ccctgcccga cccgggtccct gtgctggctc ctgcctctcc 540
tgctttttga gccanggggc aggaagtggc nenggtngtg gctggaaagc aaaacccctt 600
cctgttggtg tcccacccat ggagcccctg gggcgagccc angaacttga ncttttttgt 660
tntcttccc
669

```

```

<210> 17
<211> 697
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 33, 48, 50, 55, 59, 60, 76, 77, 78, 90, 113, 118, 130, 135,
141, 143, 150, 156, 166, 167, 170, 172, 180, 181, 190, 192,
194, 199, 201, 209, 212, 224, 225, 230, 233, 234, 236,
242, 244, 251, 253, 256, 268, 297, 305, 308, 311, 314
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 315, 317, 322, 324, 327, 333, 337, 343, 362, 364, 367, 368,
373, 384, 388, 394, 406, 411, 413, 423, 429, 438, 449, 450,
473, 476, 479, 489, 491, 494, 499, 505, 507, 508, 522, 523,
527, 530, 533, 535, 538, 539, 545, 548, 550, 552, 555
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 562, 563, 566, 568, 572, 577, 578, 580, 581, 591, 594, 622,
628, 632, 638, 642, 644, 653, 658, 662, 663, 665, 669, 675,
680, 686, 689
<223> n = A,T,C or G

```

```

<400> 17
gcaagatatg gacaactaag tgagaaggtg atnctctact gctctagntn ctcnngcnn 60
gacgcgtgta ggagannnac gctggcccan ctgcgcgcca cacacgggga tcntggtnat 120
gctgcccann gggancccca ncnctcggan ccatntcacc acccgnnccn tncgccacn 180
nctgtgctcn cncngcceng nccagctcnc gnccccctcc gccnnnctcn ttncntctc 240
cnccccctcc ncnacnacct cctaccnccg gctcccctcc cagccccccc gcgaancct 300
ccacnacncc ntcnncncga ancnccnctc gcnctengcc cngccccctt gcccccgcc 360
cncnacnncg cgnctccccg cgnccgcngc ctncccccct ccacnacag ncncccccgc 420
agnccgcnc tcgcgccnct gacgcccann cccgcgcgct tcaccttcac ggnccnaccg 480
ccccgctcnc ncnctgcnc gcgcgcnngg cgcgcccgcc cncnccgntn cncnccngnt 540
cccnccngn angcnctgcn cncnccngnc gngccgncnn ncacctcccg ncncccgccc 600
cgcccgctgg gggctcccg cncgcggnct antcccncc ctnnccgcca ctncccgntc 660
cncnctcnc gctnccgcn cgcncncnc ccccccc
697

```

```

<210> 18
<211> 670
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 234, 292, 329, 437, 458, 478, 487, 524, 542, 549, 550, 557,
576, 597, 603, 604, 646, 665
<223> n = A,T,C or G

```

```

<400> 18
ctgctgtgtaa ggggtgcagta cctaagccgg agcggggtag aggcggggcg gcaccccctt 60
ctgacctcca gtgccgccgg cctcaagatc agacatggcc cagaacttga acgacttgcc 120
gggacggctg ccgcgggggc ccgcggggcat gggcacggcc ctgaagctgt tgctgggggc 180
ggcgccgctg gctcactggg tgccggaatc tgtgttccac gtggaaggcg ggcnccagag 240
catcttcttc aatcggaatg gtggagtgc caggacacta tcctggggcg anggccttca 300
cttcaggatc ctgtgttcca gtaccccanc atctatgaca ttccggccag acctgaaaaa 360
aatctcctcc ctacaggctc caaagaaccta cagatgggtg atatctccct gcgagtgttg 420
tctcgaccaa tgctcangaa ctctctaaca tgttccangc octaagggctt ggaactacnaa 480
gaacgantgt tgcgctccat tgtcacgaag tcttcaagaa tttngtggcg caagtccaat 540
gncttcacnn ctgatcnccc agcggggcca agttanccct ggttgatccc cgggganctg 600
acnnaaaagg gccaaaggat tcccctcacc ctggataatg tggcmtccac aaagctcaac 660
tttanccacc
670

```

```

<210> 19
<211> 606
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 506
<223> n = A,T,C or G

```

```

<400> 19
actagtgcga acctcagctc ccaggccagt tctctgaatg tcgagagagt ccaggatctc 60
tgccctcagt tgtccttggt tattgatggg ggacaaattg gggatggcca gagcccgcag 120
tgtgcctctg gctcaactgt ggttgatttg tctgtgcccg gaaagtttgg catcattcgt 180
ccaggctgtg ccttggaag tactacagcc atcctccaac agaagtacgg actgctcccc 240
tcacatgcgt cctacctgtg aaactctggg aagcaggaa gcccagacc ttgtgtctgga 300
tactatgtgt ctgtccactg acgactgtca aggcctcatt tgcagaggcc accggagcta 360
gggcactagc ctgactttta aggcagtgtg tctttctgag cactgtagac caagcccttg 420
gagctgctgt tttagccttg caccctggga aaggatgtat ttatttgat ttctatatat 480
cagccaaaaa ctgaatggaa aagttagnaa cattctcag tggccttatt ctaataagtt 540
tctctgtctt gttttgtttt tcaattgaaa agttattaaa taacagattt agaactcagt 600
gagacc
606

```

```

<210> 20
<211> 449
<212> DNA
<213> Homo sapiens

```

```

<400> 20
actagtaaac aacagcagca gaaacatcag tatcagcagc gtcgccagca ggagaatatg 60
cagcgccaga gccgaggaga acccccgctc cctgaggagg acctgtccaa actcttcaaa 120
ccaccacagc cgccctgcag gatggactcg ctgctcattg caggccagat aaacacttac 180
tgccagaaca tcaaggagtt cactgcccaa aacttaggca agctcttacc ggcccaggct 240
cttcaagaat acacaacta agaaaaggaa gtttccagaa aagaagttaa catgaacctc 300
tgaagtccca ccagggcaac tcttggaaga aatatatttg catattgaaa agcacagagg 360
attctcttag tgtcattgcc gattttggct ataacagtgt ctttctagcc ataataaaa 420
aaaaaaaat cttgactgct tgcctcaaaa
449

```

```

<210> 21
<211> 409
<212> DNA
<213> Homo sapiens

```

```

<400> 21
tatcaatcaa ctgtgtgaata attaaacaat gtgtgtgtgtg atcatacaaa ggggtaccact 60
caatgataaa aggaacaagc tgcctatatg tggaaacaaca tggatgcatt tcagaaacctt 120
tatgtttgagt gaaagaacaa acacggagaa catactatgt gtttctcttt atgtaaacatt 180
acagaaataa aaacagaggc aaccacacctt gaggcagtat ggagtggagt agactggaaa 240
aaggaaaggaa ggaacctcta cgctgatgga aatgtctgtg tcttcattgg gtggtagtta 300
tgtggggata tacatttgtc aaaattttat gaactatata ctaaaagaact ctgcatttta 360
ttgggatgta aataatacct caattaaaaa gacaaaaaaa aaaaaaaa 409

```

```

<210> 22
<211> 649
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 263, 353, 610, 635, 646
<223> n = A,T,C or G

```

```

<400> 22
acaattttca ttatcttaag cacattgtac atttctacag aacctgtgat tattctcgca 60
tgataaggat ggtacttgca tatgtgtgaat tactactgtt gacagtttcc gcagaaatcc 120
tatttcaagt gaccaacatt gtggcatggc agcaaatgcc aacattttgt ggaatagcag 180
caaatctaca agagaccctg gttggttttt cgtttttgtt totttgtttt ttcccctctc 240
tctgaaatca gcagggatgg aangagggta ggggaagtat gaattactoc ttccagtagt 300
agctctgaag tgtcacattt aatatcagtt ttttttaaac atgattctag ttnaatgtag 360
aagagagaag aaagagggaag tgttcaactt ttttaacac tgatttagaa atttgatgto 420
ttatatcagt agttctgagg tattgatagc ttgctttatt tctgccttta cgttgacagt 480
gttgaagcag ggtgaataac tagggggaata tatatttttt tttttttgaa gctgtttcoa 540
gatgttttct ttggaatttc cggataagtt caggaaaaca tctgcatggt gttatctagt 600
ctgaagttcn tatccatctc attacaacaa aaacnccacg aacggnntg 649

```

```

<210> 23
<211> 669
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 642, 661
<223> n = A,T,C or G

```

```

<400> 23
actagtgcgc tactggctga aatccctgca ggaccaggaa gagaaccagt tcagactttg 60
tactctcagt caccagctct ggaattagat aaattccttg aagatgtcag gaatgggac 120
tatcctctga cagccttttg gctgcctcgg cccagcagc cacagcagga ggaggtgaca 180
tcactctgtc tgcctccctc tgtcaagact ccgacacctg aaccagctga ggtggagact 240
gcgaaggtgg tgcgtatgca gtgcaacatt gactcgtgtg agggaggagt caaacaccac 300
ctgacacttc tgcgtgaagt ggaggacaaa ctgaaccgcg acctgagctg tgacctgatg 360
ccaaatgaga atatcccccga gttggcggct gagctgggtc agctgggctt cattagtgtg 420
gctgaccaga gccggttgac ttctctgcta gaagagaact gaacaagtcc aattttgcaa 480
ggaacagtac cctcaactca gccgctgtca ccgtctcttc tttagagctca ctggggccag 540
gccctgatct gcgctgtggc tbtctgggac gtgctgcacc ctctgtctct ccccccagtc 600
agtattacct gtgaagccct tccctccttt attattcagg anggctgggg gggctccttg 660
nttctaacc 669

```

```

<210> 24
<211> 442

```

<212> DNA
<213> Homo sapiens

<400> 24
actagtaccac tcttgacaga ggatacatgc tcccaaaacg tttgttacca cacttaaaaa 60
tcactgccat cattaagcat cagtttcaaa attatagcca ttcgatgttt actttttcca 120
gatgacatc attattctag tcctttgaat ttgtaagggg aaaaaaaca aaaacaaaaa 180
cttaagatgc acttttctcc agcacatcag atttcaaatt gaaatttaa gacatgctat 240
ggtaatgcac ttgctagtac tacacacttt ggtacaacaa aaaacagagg caagaacaaa 300
cggaagagaga aaagccttcc tttgttggcc cttaaacctga gtcaagatct gaaatgtaga 360
gatgactctc gacgatacct gtatgttctt attgtgtaaa taaaattgct ggtatgaaat 420
gacctaaaaa aaaaaaaga aa 442

<210> 25
<211> 656
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 330, 342, 418, 548, 579, 608
<223> n = A,T,C or G

<400> 25
tgcaagtacc acacactgtt tgaattttgc acaaaaagtg actgtaggat cagggtgatag 60
ccccggaatg tacagtgtct tgggtcacca agatgccttc taaaggctga cataccttgg 120
accctaattg ggcagagagt atagccctag cccagtgggt acatgaccac tccctttggg 180
aggcctgagg tagaggggag ttgtatgtgt tttctcagtg gaagcagcac atgagtgggt 240
gacaggatgt tagataaagg ctctagttag ggtgtcattg toatttgaga gactgacaca 300
ctcttagcag ctggtaaagg ggtgctggan gccatggagg anctctagaa acattagcat 360
gggctgactc gattacttcc tggcatcccg ctacacttta tgggaagtct tattagangg 420
atgggacagt ttccatctc ctgtctgttg agctctggaa cactctctaa atttccctct 480
attaaaaatc actgccttaa ctacacttcc tcttgaagg aatagaaatg gaactttctc 540
tgacatannt cttggcatgg ggagccagcc acaaatgana atctgaacgt gtccagggtt 600
ctcctganac tcacttacat agaattgggt aaacccctcc ttggaataag gaaaaa 656

<210> 26
<211> 434
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 395
<223> n = A,T,C or G

<400> 26
actagttcag actgccacgc caaccocaga aaataccoca catgccagaa aagtgaagtc 60
ctaggtgttt ccatctatgt tcaatctgt ccatctacca ggctctgcga taaaaacaaa 120
acaaaaaaac gctgccaggt tttagaagca gttctggtct caaaaccatc aggatcctgc 180
caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggcttt cacttcatct 240
aataactgaa ttgtcaggct ttgattgata attgtagaaa taagtacgct tctgtttgtg 300
gaataagtta taatcagtat tcactctctt gttttttgtc actcttttct ctctaatgtt 360
gtcatttgta ctgtttgaaa aatatttctt ctatnaaatt aaactaacct gccttaaaaa 420
aaaaaaaaaa aaaa 434

<210> 27
<211> 654

<212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 505, 533, 563, 592, 613, 635, 638
 <223> n = A,T,C or G

<400> 27
 actagtccaa cacagtcaga aacattgttt tgaatcctct gtaaaccaag gcattaatct 60
 taataaacca ggatocattt aggtaccact tgatataaaa aggatatacca taatgaatat 120
 ttataactgc atcctttaca tttagccacta aatcgtttat tgcttgatga agacctttca 180
 cagaatccta tggattgcag catttcaactt ggctaactca taccocatgcc ttaagagggg 240
 gcagttttctc aaaagcagaa acatgcgccgc agttctcaag ttttctctct aactccattt 300
 gaatgtaagg gcagctgggc cccaatgtgg ggaggtccga acattttctg aattcccat 360
 ttattgttgc cggctaaatg acagttttctg tcattactta gattccgatc tttcccaag 420
 gtgttgattt acaagagggc cagctaatag cagaaatcat gacctgaaa gagagatgaa 480
 attcaagctg tgagccaggc agganctcag tatggcaaaag gtcttgagaa tngccattt 540
 ggtcacaaaa aaatttttaa gcntttatgt tataccatgg aaccatagaa anggcaagg 600
 aattgttaag aanaatttta agtgtcocga ccanaanga aaaaaaaaaa aaaa 654

<210> 28
 <211> 670
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 101, 226, 274, 330, 385, 392, 397, 402, 452, 473, 476, 532,
 534, 538, 550, 583, 595, 604, 613, 622, 643, 669
 <223> n = A,T,C or G

<400> 28
 cgtgtgcaca tactggggagg atttccacag ctgcacggtc acagccctta cggattgcc 60
 ggaagggggc aaagatatgt gggataaact gagaaaagaa nccaaaaacc tcaacatcca 120
 aggcagctta ttcgaaactct gcggcagcgg caacgggggc gcggggctcc tgctcccgcc 180
 gttcccggtg ctctctggtgt ctctctcggc agcttttagc acctgntttt cctctgagc 240
 gtggggccag ctccccccgc gcgcgccacc cactctcact coactgtccc ggaaatcgag 300
 aggaagatca ttatgttctt ggggaacttn gtgattctct gtgatgtgta aaaacactca 360
 tataggyaat gtgggaaatc ctganctctt tnttatntcg tntgatitct tgtgttttat 420
 ttgcccanaa gttaccaatc agtgaccaac cnagcacagc caaaaaatcg acntongctt 480
 tagtccgtct tcacacacag aataagaaaa cgccaaaccc accccattt tnannttnat 540
 tattactaan tttttttctg ttggcnaaag aatctcagga acngccctgg ggccnccgta 600
 ctanagttaa ctnagctagt tncatgaaaa atgatgggct cncctcaat gggaaagcca 660
 agaaaaagnc 670

<210> 29
 <211> 551
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 336, 474, 504, 511, 522, 523, 524, 540, 547
 <223> n = A,T,C or G

<400> 29
 actagtctct cacagcctgt gaatccccc agaccttca agcatagtga gcggagaaga 60

```

agatctcagc gtttagccac cttaccatg cctgatgatt ctgtagaaaa ggtttcttct 120
ccctctccag ccaactgatgg gaaagtattc tccatcagtt ctcaaaatca gcaagaatct 180
tcagtaccag aggtgcctga tgttgacatc ttgccacttg agaagctggg accctgtctc 240
cctcttgact taagtctgtg ttccagaagtt acagcaccgg tagcctcaga ttctctcttac 300
cgtaaatgaat gtccccagggc agaaaaagag gatacnacga tgcctccaaa tcttctctcc 360
aaagcaatag ctgatgggaa gaggagctcc agcagcagca ggaatatoga aaacagaaaa 420
aaaagtgaaa ttgggaagac aaaagctcaa cagcatttgg taaggagaaa aganaagatg 480
aggaaggaa agagaagaga gacnaagatc nctacggacc gnnnccggaa aagaagaagn 540
aaaaanaaa a
551

```

```

<210> 30
<211> 684
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 545, 570, 606, 657, 684
<223> n = A,T,C or G

```

```

<400> 30
actagttcta tctggaaaaa gccggggttg gaagaagctg tggagagtc gtgtgcaatg 60
cgagactcat ttcttggaag catccctggc aaaaatgcag ctgagtagca ggttatcact 120
gtgatagaac ctggactgct ttttgagata atagagatgc tgcagttcga agagactctc 180
agcacctctc agttgaatga attaatgatg gcttctgagt caactttact ggctcaggaa 240
ccacagagaga tgactgcaga tgtaatcgag cttaaaagga aattctctcat caacttagaa 300
gggtgtgata ttctgtgaaga gtcttccat aaagtaattg tcatgccgac tacgaaagaa 360
aaatgccccc gttgttgaa gtatacagcg ggagtcttca gatacactgt gtctctgatg 420
tgcagaagtt gtcagtggga aatatgtatt aacagctcac tcgagcaaga accctcctga 480
cagtagctgg ctgagaagtt ggatggatta ttacaatat aggaagaaaa gccagaatt 540
aggtnatgag tggatgagta aatgggtgga gatggggaat tcaaatcaga attatggaag 600
aagtnttcc tgttactata gaaaggaatt atgtttattt acatgcagaa aatatanatg 660
tgtgtgtgt accgtggatg gaan
684

```

```

<210> 31
<211> 654
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 326, 582, 651
<223> n = A,T,C or G

```

```

<400> 31
ggcagaaaaa ggaaccaata ttccagaaac aagcttaata ggaacagctg cctgtacatc 60
aacatcttct cagaatgacc cagaagttat catcgtggga ctggcgtgc ttgctctgc 120
tttggcagct gtgctttcca gagatggaag aaaggtgaca gtcattgaga gagacttaaa 180
agagcctgac agaataagtg gagaattctc gcagccgggt ggttatcatg ttctcaaaag 240
ccttggtctt ggagatacag tggaaagttc tgatgccag gttgtaaatg gttacatgat 300
tcatgatcag ggaagcaaa tcagangttc agatctctta cctctgtcga gaaaaaatc 360
aagtgcagag tggaaagact ttccatcacg gaagattcat catgagtctc cggaaagcag 420
ctatggcaga gcccaatgca aagtttatgt aaggtgtgtg gttacagta ttagggaag 480
atgatgttgt gatggagatt cagtacaagc ataaagagac tgggagatat caaggaaact 540
catgctccac tgactgttgt tcgacatggg cttttctcca anttcaggaa aagcctggct 600
tcaataaagt ttctgtatca ctcatcttgg tggctttctta tgaagaatgc nccc 654

```

```

<210> 32

```


<211> 673
 <212> DNA
 <213> Homo sapiens
 <220>
 <221> misc_feature
 <222> 376, 545, 627
 <223> n = A,T,C or G

<400> 32
 actagtgaag aaaaagaatg totgatacgg gacaaaaatg ctcttcaaaa catcattctt 60
 tatcacotga caccaggagt ttctattgga aaaggatttg aacctgggtg tactaacatt 120
 ttaaaagacca cacaaggaga caaaatcttt ctgaaagaag taaatgatac actctctggtg 180
 aatgaattga aatcaaaaga atctgacatc atgacacaaa atgggtgtaat tcatgttgta 240
 gataaacctc tctatccagc agacacacct gtgtgaaatg atcaactgct ggaaatactt 300
 aataaattaa tcaaatacat ccaaatatag ttgttctgtg gtgacacctt caaagaaatc 360
 cccgtgactg tctatnagcc aattattaaa aaatacacca aaatcattga tgggaagtgc 420
 tgtgggaaat aactgaaaaa gagaccgaga agaacgaatc attacaggct ctgaaataaa 480
 ataccataga ttctactcgg aggtggagaa acagaagaac tctgaagaaa ttgttacaag 540
 aagangtccc aaggtcacca aattcattga aggtgggtgat ggtctttatt tgaagatgaa 600
 gaatttaaaa gacgcttcag ggagacnccc catgaaggaa ttgccagcca caaaaaatt 660
 cagggttagg aaa 673

<210> 33
 <211> 673
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 325, 419, 452, 532, 538, 542, 571, 600, 616, 651, 653, 672
 <223> n = A,T,C or G

<400> 33
 actagttatt tactttctc cgcttcagaa ggtttttcag actgagagcc taagcatact 60
 ggaatctgtt ttcttttttg gtctcacctc atcagtggtc atagtggtgag aaattataaa 120
 gaaggttgaa agggagcagg aaaagatcca gaagcatggt agttcgacat catcatcttt 180
 tcttgaagta tgaatcatat tgcattattt tatttgcaaa ctagggaattg cagtctgagg 240
 atcatattga agggcaagtt caagaggata tgaagatttg agaacttttt aactattcat 300
 tgaactaaaa tgaacattaa tgttnaagac ttaagacttt aacctgctgg cagtcccaaa 360
 tgaattatgt caactttgat atcatattcc ttgattttaa ttgggctttt gtgattgant 420
 gaaactttat aaagcatatg gtcagttatt tnattaaaaa ggcaaaacct gaaccacctt 480
 ctgcaactaa agaagtctaa cagtaacaat acctatctat cttagatgga tnatattntt 540
 tnatatttta aatatgtgac tatttatggt nggtggggct ttctactaa tacacaaatn 600
 aatttatcat ttcaanggca ttctatttgg gtttagaagt tgattccaag nantgcata 660
 ttcgtactgt tnt 673

<210> 34
 <211> 684
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 414, 472, 480, 490, 503, 507, 508, 513, 523, 574, 575, 598,
 659, 662, 675
 <223> n = A,T,C or G

```

<400> 34
actagtttat tcaagaaaag aacttactga ttctctgtgt cctaaagcaa gagtggcagg 60
tgactcagggc tgggtgtagca tccggttcct ttagtgccag taactgcatt tgcactgat 120
gaccaaaggag gaatacacta agacatttga gaagcagtggt tatgaacgtt cttggacaag 180
ccacagttctt gagccttaac cctgtagttt gcacacaaga acgagctcca cctccctctc 240
ttcaggagga atctgtgcgg atagattggc tggacttttc aatggttctg ggttgcaagt 300
gggcactgtt atggctgggt atggagcgga cagcccgagg aatcagagcc tcagcccgcc 360
tgccgtggtt gaaggtacag gtgttcagca ccttcggaaa aagggcataa agtngtgggg 420
gacattcttc agtccaagaa gaatgcattg accattgctg gctatttctc tncctagtan 480
gaattggatn catttttgac cangatnntt ctncctatgct tntttgcaat gaaatcaaat 540
ccgcatttat ctacaagtgg tatgaagtcc tgcnnccccc agagagctg ttcaggcnat 600
gtcttccaag ggcagggtgg gttacaccat tttaacctcc ctctccccc agattatgna 660
cncagaaggga attnttttc tccc 684

```

```

<210> 35
<211> 614
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 17, 20, 152, 223, 267, 287, 304, 306, 316, 319, 321, 355,
365, 382, 391, 407, 419, 428, 434, 464, 467, 477, 480, 495,
499, 505, 515, 516, 522, 524, 527, 542, 547, 549, 567, 572,
576, 578
<223> n = A,T,C or G

```

```

<400> 35
actagtccaa cgcgttngon aatattcccc tggtagccta ctctcttacc ccogaatatt 60
ggtaagatcg agcaatggct tcaggacatg ggttctcttc tctgtgtatc attcaagtgc 120
tcactgcgatc aagactggct tgtctcagtg tntcaacctc accagggctg tctcttggtc 180
cacacctcgc tcctctgttag tcgcgtatga cagcccccat canatgacct tggccaagtc 240
acggtttctc tgtggtcaat gttggtnggc tgattggtgg aaagtanggt ggaccaagg 300
aagncnctgc agcagncanc nccagttctg caccagcagc gcctccgtcc tactnggggtg 360
ttccngtttc tcttggccct gngtgggcta nggcctgatt ogggaaanag cctttgcaag 420
gaagggganga taantgggat ctaccaattg attctggcaa aacnatntct aagattnttn 480
tgctttatgt ggganacana tctanctctc atttnttctg gnanatnaca cctactcgt 540
gntcgancnc gtcttcgatt ttccgganaca cnccantnaa tactggcggt ctgttgttaa 600
aaaaaaaa aaaa 614

```

```

<210> 36
<211> 686
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 222, 224, 237, 264, 285, 548, 551, 628, 643, 645, 665, 674
<223> n = A,T,C or G

```

```

<400> 36
gtggctggcc cgggttctcg cttctcccca tccctacttt tctctccctc ctccctttcc 60
ttacctcgtc gactgttgct tgctggctgc agactcctg accctctcct caccctctcc 120
taacctcgtt gccacgggat tgcccttctt tctctgttgc ccagcccagg cctagtgtca 180
gggggggggg cttggagcagc ccgaggaact cgagcagaag anaaaaaaga cagacnaac 240
ctcagctcgc cagtcggctc gctngcttcc cgcgcgatgg caatnagaca gacgcgcgtc 300
acctgctctg ggcacacgag acccgtggtt gatttggcct tcagtggcat cacccttatg 360
ggtatttctt atcagcgct tgcaaatag gttaacctat gctacgcag ggagatcacag 420

```

```

gagactggat tggaacattt ttggggctcta aaggtctgtt tgggggtgcaa cactgaataa 480
ggatgccacc aaagcagcta cagcagctgc agatttcaca gcccaagtgt gggatgctgt 540
ctcagganat naattgataa cctggcctcat aacacattgt caagaatgtg gatttcccca 600
ggatattatt atttgtttac cggggganag gataactgtt tcnctattt taattgaaca 660
aactnaaca aanctaagg aaatcc 686

```

```

<210> 37
<211> 681
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 7, 10, 11, 19, 25, 32, 46, 53, 77, 93, 101, 103, 109, 115,
123, 128, 139, 157, 175, 180, 192, 193, 194, 212, 218, 226,
227, 233, 240, 241, 259, 260, 267, 289, 296, 297, 298, 312,
313, 314, 320, 325, 330, 337, 345, 346, 352, 353, 356
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 382, 385, 400, 427, 481, 484, 485, 491, 505, 515, 533, 542,
544, 554, 557, 560, 561, 564, 575, 583, 589, 595, 607, 619,
628, 634, 641, 645, 658, 670
<223> n = A,T,C or G

```

```

<400> 37
gagacanaac naacgtcang agaanaaaag angcatggaa cacaanccag gncgatggc 60
caccttccca ccagcancca gcgcccccca gcngcccca ngncggang accangactc 120
cancctgnat caactgtanc tctattctcg gccatnctt acctcgagg tggangccgm 180
aaaggtcgca cnnncagaga agctgctgcc ancaccancc gcccnncctc tgnccggctn 240
nataggaaac tggtagacnn gctgcanaat tcatacagga gcacgcgag ggcacnnnct 300
cacactgagt tnnngatgan gcctnaaccan ggacctnccc cagcnnnattg annacnggac 360
tgcggaggaa ggaagacccc gnaacggatc ctggccggcn tgccaccccc ccaccctag 420
gattatnccc cttgactgag tctctgaggg gctacccgaa ccgcctcca ttccctacca 480
natnntgctc natcgggact gacangctgg ggatnggagg ggctatcccc cancatcccc 540
tnanaccaac agcnacngan natnggggct ccccnnggtc gngcaacnc tcctncccc 600
cggcgcnngc cttcggtgnt gtctctcctc aacnaattcc naaanggcgg gcccccngt 660
ggactcctcn ttgttccctc c 681

```

```

<210> 38
<211> 687
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 3, 30, 132, 151, 203, 226, 228, 233, 252, 264, 279, 306,
308, 320, 340, 347, 380, 407, 429, 437, 440, 445, 448, 491,
559, 567, 586, 589, 593, 596, 603, 605, 606, 609, 626, 639,
655, 674, 682
<223> n = A,T,C or G

```

```

<400> 38
canaaaaaaa aaaacatggc cgaaccagn aagctgcgag atggcgccac ggccccctctt 60
ctcccgccct gtgtccggaa ggtttccctc cgaggcgccc cggctccccc aagcggagga 120
gagggcgagg cntgcccggg ccggagctca naggccctgg ggccgctctg ctctcccgcc 180
atcgcaaggg cggcgctaac ctanaggctc cccgcaaaag tccccnangc gngggcgggc 240
gggggctgtg anaaccgcaa aaanaacgct gggcgcgcn gcaaccogtc cacccccggc 300

```

```

aagganacac ttccacagan gcagcggttc cacagcccan agccacnttt ctagggtgat 360
gcaccccaagt aagttccctgn cggggaagct caccgtgtgc aaaaaancctc ttgcctccac 420
cgggcgacacna agggggangan ggccangancg tgcccgccgcg acaggtcctac tgatcacgtc 480
gcccgcoccta ntctgctttt gtgaatctcc actttgttca accccaccgcg ccgttctctc 540
ctccttgccg cttcctctna ccttaanaac cagcttctc taccconatng tanttctctc 600
gcnncnngng aaaaataatc ggtccnccgg aacctcttnc ctgtgggcaac tgcctnaaaa 660
aactgctgtt ctgnttactg cngtccc

```

```

<210> 39
<211> 695
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 300, 401, 423, 429, 431, 437, 443, 448, 454, 466, 492, 515,
523, 524, 536, 538, 541, 552, 561, 566, 581, 583, 619, 635,
636, 641, 649, 661, 694
<223> n = A,T,C or G

```

```

<400> 39
actagtctgg cctacaatag tgtgattcat gtaggacttc ttcatcaat tcaaaacccc 60
tagaaaaacg tatcacagatt atataagtag ggataagatt tctaacattt ctgggctctc 120
tgacccctgc gctagactgt ggaaggggag tattattata gtatacaaca ctgctgttgc 180
cttattagtt ataactgat aggtgctgaa ttgtgtacca caatttaaaa acactgtaat 240
cgaacttttt ttttttaact gtatgcacg catgtgaatg ttaatgttaa ttgttccaan 300
gtgtttatgg gtagaaaaaa ccacatgcct taaaatttta aaaagcaggg cccaaactta 360
ttagtttaaa atagggggta tgtttccagt ttgttattaa ntgggtatag ctctgtttag 420
aanaaatcna ngacacangat ttngaaantt aagntgacat tatttncag tgaactgtta 480
atttgaatct anacacgcgca ccttccgttt tggtnctatt ggntttgaa tccaaanccg 540
ntccaaatct ntctggaac ngtccnttta acttttttac nanactctat tttttttatt 600
tggaaatggc ctatttaang ttaaaaaggg ggggnnccac naccattctt gaataaaact 660
naatatatat ccttgggtccc ccaaaattta aggnng

```

```

<210> 40
<211> 674
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 403, 428, 432, 507, 530, 543, 580, 583, 591, 604, 608, 621,
624, 626, 639, 672
<223> n = A,T,C or G

```

```

<400> 40
actagttagc agttgggagt ggttgctata ccttgacttc atttatatga atttccactt 60
tattaaataa tagaaaagaa aatcccggtg cttgcagtag agttatagga cattctatgc 120
ttacagaaaa tatagccaat attgaaatca aatagtaaag gctgttctgg ctttttatct 180
tcttagctca tcttaataa gtagtacact tgggatgcag tgcgtctgaa gtgctaatca 240
gttgtaacaa tagcaaaat cgaacttagg atgtgtttct tctcttctgt gtttcgattt 300
tgatcaattc ttttaatttg ggaacctata atacagtttt cctattcttg gagataaaaa 360
ttaaattgat caactgatatt taagtcaatt tgccttctcat ctnaatattc catattctgt 420
attaggnana antacctccc agcacagccc cctctcaaac cccacccaaa accaagcatt 480
tggaaatgagt ctcctttatt tcogaantgt ggaatgttata acccatatcn ctocaaattc 540
tgntttgggt ggttattaat ttgaactgtg catgaaaagn ggnaactctt nctttgggtc 600
aaantttncg gggttaattg nctngncaaa tccaatttnc ttttaagggtg tctttataaa 660
atttgctatt cngg

```

<210> 41
 <211> 657
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 243, 247, 251, 261, 267, 272, 298, 312, 315, 421, 432, 434,
 501, 524, 569, 594, 607, 650
 <223> n = A,T,C or G

<400> 41
 gaaacatgca agtaccacac actgttttgaa ttttgacaaa aaagtgactg tagggatcag 60
 gtgatagccc cggaatgtac agtgtcttgg tgcaccaaga tgccttctaa aggcgtgacat 120
 accttggggac cctaattggg cagagagtat agccctagcc cagtgggtgac atgaccacto 180
 ccttggggag gctgaagtta aaggggaatgg tatgtgtttt ctcagtgaag cagcacatga 240
 atnggttnaca ngatgttaaa ntaaggntct antttgggtg tcttgtcatt tgaaaaaantg 300
 acacactcct ancanctggg aaaggggtgc tggagccat ggaagaactc taaaaacatt 360
 agcatggggt gatctgatta ctctcctggc tcccgctcac ttttatggga agtcttatta 420
 naaggatggg anaattttcc atatccttgc tgttggaaact ctggaacact ctctaaattt 480
 cctcttatta aaaaactgct nctttactac acttctctct tgangaata gaaatggacc 540
 tttctctgac ttagtcttgg gcattggganc cagcccaaat taaaatctga cttntccggt 600
 ttctcngaa ctcacctact tgaattggta aaacctcctt tgaattagn aaaaacc 657

<210> 42
 <211> 389
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 179, 317, 320
 <223> n = A,T,C or G

<400> 42
 actagtctgt aggaatgtaa acaagtttgc tgggccttgc gagacttcac caggttgttt 60
 cgatagctca cactcctgca ctgtgctgtg caccaggaa tgtctttttt aattagaaga 120
 caggaaagaaa acaaaaacca gactgtgtcc cacaatcaga aacctcgtt gtggcagang 180
 ggccttcacc gccaccaggg tgtcccgcca gacagggaga gactccagcc ttctgaggcc 240
 atcctgaaga attcctgttt ggggggttgt aaggaaaac acccggtatt aaaaagatgc 300
 tttgctctgc cgcgctngtn ggggaaggagc tggtttctgt gtgaatttct taaaagaaaa 360
 atattttaag ttaagaaaaa aaaaaaaaaa 389

<210> 43
 <211> 279
 <212> DNA
 <213> Homo sapiens

<400> 43
 actagtgcac agctcctggt ctgagatgt cttctgttta aggagatggg ccttttggag 60
 gtaaaaggata aaatgaatga gttctgtcat gattcactat tctagaactt gcatgacctt 120
 tactgtgttta gctctttgaa tgttcttgaa attttagact tctcttgtaa acaaaataa 180
 tgtccttatc attgtataaa agctgttatg tgcaacagtg tggagatcct tgtctgattt 240
 aataaaatc ttaaacactg aaaaaaaaaa aaaaaaaaaa 279

<210> 44
 <211> 449

<212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 245, 256, 264, 266, 273, 281, 323, 325, 337, 393
 <223> n = A,T,C or G

<400> 44
 actagtagca tcttttctac aacgttaaaa ttgcagaagt agcttatcat taaaaaaca 60
 caacaacaac aataacaata aatcctaagt gtaaatcagt tattctaccc cctaccaagg 120
 atatacagcct gtttttctcc ttttttctcc tgggaataat ttgtgggcttc ttcccaaat 180
 tctacagcct ctttctctct ctcctgcttg agcttccctg ttgtgcacga tgcgtgtgtgc 240
 aagantgggc tgtttngctt ggantnoggc ccnagtggaa ncatgcttcc cctgtgtact 300
 gttggaagaa actcaaacct tonancccta ggtgttcca ttttgtcaag tcatcactgt 360
 atttttgtac tggcattaac aaaaaaagaa atnaaatatt gttccattaa actttaataa 420
 aactttaaaa gggaaaaaaa aaaaaaaa 449

<210> 45
 <211> 559
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 263
 <223> n = A,T,C or G

<400> 45
 actagttggg gggaatcacg gacacttaaa gtcaatctgc gaaataattc ttttattaca 60
 cactcaactga agttttttgag tcccagagag ccattctatg tcaaacattc caagtactct 120
 ttgagagccc agcattacat caacatgccc gtgcagttca aaccgaagtc cgcaggcaaa 180
 tttgaagcct tgcttgtcat tcaaacagat gaaggcaaga gtattgtcat tgcactaat 240
 ggtgaagctc ttggaaaaaa tttnactagaa tactttttgt gttaagttaa ttacataagt 300
 tgtattttgt taactttatc tttctacact acaattatgc ttttgtatat atattttgtga 360
 tgatggatat ctataattgt agattttgtt tttaacaagc aatactgaag actcgactga 420
 aatattatgt atctagccca tagtattgta ctttaactttt acaggggtgaa aaaaaaatc 480
 tgtgtttgca ttgattatga tattctgaat aaatatggga atatatttta atgtgggtga 540
 aaaaaaaaaa aaaaaggaa 559

<210> 46
 <211> 731
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 270, 467, 477, 502, 635, 660, 671, 688, 695, 697, 725
 <223> n = A,T,C or G

<400> 46
 actagttcta gtaccatggc tgtcatagat gcaaccatta tattccattt agtttcttcc 60
 tcaggttccc taacaattgt ttgaaactga atatatatgt ttatgtatgt gtgtgtgttc 120
 actgtcatgt atatggtgtga tatgggatgt gtgcagtttt cagttatata tatattcata 180
 tatacatatg catatatatg tataatatat atatatatcat gcatacaact gtataatata 240
 catatatata cacatatatg cacacatatn atcactgagt tccaagtga gtctttattt 300
 ggggcaattg tattctctcc ctctgtctgc tcaactgggc ttgtcaagac atagcaattg 360
 cttgatttcc ttggataag agctcttatc tcggcaactc tgactctagc ctttaacttta 420

```

gatttctatt ccagaatacc tctcatatct atcttaaaac ctaaganggg taaagangtc 480
ataagattgt agtatgaag antttgctta gttaaattat atctcaggaa actcattcat 540
ctacaaatta aattgtaaaa tgatgggttg ttgtatctga aaaaatgttt agaacaagaa 600
atgtaactgg gtacctgtta tatcaaaagaa cctcnattta ttaagtctcc tcatagccan 660
atccttatat ngccctctct gacctgantt aatananact tgaataatga atagttaatt 720
taggnttggg c 731

```

<210> 47

<211> 640

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 5, 28, 106, 153, 158, 173, 176, 182, 189, 205, 210, 214,
225, 226, 229, 237, 260, 263, 269, 277, 281, 282, 322, 337,
338, 354, 365, 428, 441, 443, 456, 467, 476, 484, 503, 508,
554, 567, 575, 579, 588, 601, 606, 609, 611, 621, 636

<223> n = A,T,C or G

<400> 47

```

tgcgngcggg tttggccctt ctttgtanga cacttttcac cgccctgaaa tcttcccgat 60
cgttaataac tcttcaggto cctgcctgca caggggtttt tcttantttg ttgccataca 120
gtacaccaaa tgtgacatcc ttccaccaat atngatttnc tcataccaca tcntcnatgg 180
anacgactnc aacaattttt tgatnaccn aanaactggg ggctnnaana agtacantct 240
ggagcagcat ggacctgtcn gcnactaang gaacaanagt nntgaacatt tacacaacct 300
ttggtatgtc tttctgaag anagaaacat gcttctnncc ctgaccacg aggncaaccg 360
caganattgc caatgccaaag tccgagcggg tagatcagg aaatacattc atggatgcatt 420
taccatantc gtcccccga nanaagatgc cctaanggct tcttcanact ggtccngaaa 480
acanatcac ctgggtgctt ganaacacac tctttggaag atcatctggc acaagttccc 540
cccagtggtt tttnccttgg cacctanctt accanacna tccggaancc atcttttggc 600
ntggnttnt ntgggacca ntcttctcac aactgnaccc 640

```

<210> 48

<211> 257

<212> DNA

<213> Homo sapiens

<400> 48

```

actgatatat gaaaatgtaa atatcacttg tgtactcaaa caaaagtgtg tcttaagctt 60
ccaccttgag cagccttgga aacctaacct gctctttta gcataatcac attttctaaa 120
tgattttctt tgttctctgaa aaagtgtatt gtattagtgt tacatttgtt ttttggaaga 180
ttatatattg atatgtatca tcataaaata ttaataataa aagtatcttt agagtgaaga 240
aaaaaaaa aaaaaaa 257

```

<210> 49

<211> 652

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 410, 428, 496, 571, 647

<223> n = A,T,C or G

<400> 49

```

actagtctag atgagtggct gctgaagggg ccccttgctc attttcatta taaccaatt 60
tccactttat tgaactctta agtcataaat gtataatgac ttatgaatta gcacagttaa 120

```

```

gttgacacta gaaactgccc atttctgtat tacactatca aataggaaac attggaaaga 180
tggggaaaaa aactcttattt taaaatggct tagaaagtgt tcagattact ttgaaaaatto 240
taaacctctt tctgtttcca aaacttgaaa atatgtagat ggactcatcg attaagactg 300
ttttcaaaagc ttctctcaca tttttaaagt gtgattttcc ttttaataa catatttatt 360
ttotttaaag cagctatata ccaaccocatg actttggaga tataacctatn aaaccaatat 420
aacacgacang tatttgaagc agcttttcca aatgttgctt cagatgtgca agttgcaaat 480
tttattgtat ttgtanaata caatttttgt tttaaactgt atttcaatct atttctccaa 540
gatgcttttc atatagaagt aaatatccca ngataactgc ttctgtgtcg tgcatttga 600
cgcataactg cacaaatgaa cagtgtatata ctcttgggtg tgcattnacc cc 652

```

<210> 50

<211> 650

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 237, 270, 311, 443, 454, 488, 520, 535, 539, 556, 567, 594, 603, 634

<223> n = A,T,C or G

<400> 50

```

ttgcgctttg atttttttag ggcttgtgccc ctgttttcaat tatagggtct agaatgcttg 60
tggtgagtaa aaaggagatg cccaatatcc aaagctgcta aatgttctct ttgccaataa 120
gaactcgtgt aactgtgtga acacttggga ttttttctct ctgtcccgag gtogctgtct 180
gctttctttt ttgggttctt tctagaagat tgagaaatgc atatgacagg ctgaganaoc 240
ctcccaaac acacaagctc tcagccacac gcagcttctc cacagcccca gttcgcaac 300
ggctcctgga nggctgctg ggggagcgag acatgggagt gccaaaggtg ccagatggtt 360
ccaggactac aatgtcttta tttttaactg ttgtccactg ctgccctcac cctgcccog 420
ctctggagta cgtctgccc canacaagtg gganbgaat gggggtgggg gggaaactg 480
attccgantt agggggtgccc taactgaaca gtaggatan aaggtgtgaa cctngaanat 540
gcttttataa attatnttcc ttgttanatt tattttttaa ttaactctct gttnaactgc 600
cnnnggaaaa ggggaaaaaa aaaaaaaaaa tctnttttaa cacatgaaca 650

```

<210> 51

<211> 545

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 66, 159, 195, 205, 214, 243, 278, 298, 306, 337, 366, 375, 382, 405, 446, 477, 492, 495, 503, 507, 508, 521, 537

<223> n = A,T,C or G

<400> 51

```

tgccgtgcaa ccagggtagc tgaagtttgg gtctgggact ggagattggc cattaggcct 60
ctganaatcc cagctccctt ccaccaagcc cagtcttgct acgtggcaca gggcaaacct 120
gaactccctt gggcctcagt ttccctccc ctctcatgana tgaaaagaat actactttt 180
cttgttggtc taactntgct ggacncaaag tgtngtcatl attgttgtat tgggtgatgt 240
gtncaaaact gcagaaagct actgcctatg agaggaanta agagagatag tggatganag 300
ggacanaag agtcattatt tggatatgat ccaccctccc caactttct ctctcagtc 360
cctgcnctct atgtntctgg tntgttgagt cctttgtgcc accanccatc atgttttga 420
ttgtgcact cctgggaagg ggtgtnatcg tctcacaact tgttgtcatc gtttganatg 480
catgctttct tnatnaaaca aanaaannaa tgtttgacag ngtttaaaat aaaaaanaa 540
caaaa

```

<210> 52

<211> 678

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 98, 119, 121, 131, 136, 139, 140, 142, 143, 163, 168, 172,
176, 184, 189, 190, 191, 200, 201, 205, 207, 221, 223, 229,
230, 237, 240, 241, 255, 264, 266, 267, 276, 280, 288, 289,
291, 297, 301, 306, 308, 314, 315, 326, 332, 335, 337

<223> n = A,T,C or G

<221> misc_feature

<222> 339, 341, 343, 344, 345, 347, 350, 355, 356, 358, 362, 363, .
372, 379, 395, 397, 398, 400, 403, 412, 414, 421, 423, 431,
435, 438, 439, 450, 457, 463, 467, 471, 474, 480, 483, 484,
487, 490, 491, 492, 493, 499, 500, 504, 508, 518, 536

<223> n = A,T,C or G

<221> misc_feature

<222> 538, 549, 551, 552, 554, 556, 557, 562, 563, 567, 571, 572,
576, 579, 590, 592, 595, 598, 606, 609, 613, 620, 622, 624,
626, 631, 634, 638, 641, 647, 654, 660, 661, 674

<223> n = A,T,C or G

<400> 52

actagtagaa	gaacttttgc	gctttttgtc	ctctcacagg	cgctaaagt	cattgccatg	60
ggaggaagac	gatttggggg	gggagggggg	ggggggcang	tcctgtgggc	tttccctant	120
ntatctccat	ntccantgnn	cnntgtgcgc	tcttccctcg	tcncattnga	anttantccc	180
tggccccenn	ncctctcccn	ncctnccct	ccccctccg	ncnccctenn	ctttttntan	240
ntctcccatc	ctcctctccc	ctcnanngtc	ccaacnccg	cagcaatnnc	ncacttntct	300
ntctcncncc	tcnncctgtt	cttctntttc	cnaentntnc	ncnnntnccn	tgccnntnaa	360
annctctccc	cncgtcaanc	gattctctcc	ctcccnnnan	ctntccaact	cntnctcttc	420
ncncgtctct	nttctcnnc	ccactctctc	ccttcgnccc	cantaacnct	ncncccttn	480
cgntctctnn	nnntctctnn	accncccncc	tcccttctcc	cccttctctc	ccggtntntc	540
ctctctcccn	nnnccnccct	cnncctctcc	nngcgnccnt	ttccgccccn	cnccnccntt	600
ctctctctcc	cantccatcn	cntntnccat	netnccctcc	netcaacncc	gctncccccn	660
ntctcttcca	caacgtcc					678

<210> 53

<211> 502

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 139, 146, 215, 217, 257, 263, 289, 386, 420, 452, 457, 461,
466, 482, 486

<223> n = A,T,C or G

<400> 53

tgaagatcct	ggtgtgcgca	tggggcgcgc	ccccgcctgt	tgttaccogt	attgtaagaa	60
caagccgtac	ccaaagtctc	gcttctgcgc	aggtgtccct	gatgccaaaa	ttcgcatattt	120
tgacctgggg	cggaaaaaang	caaaaantgga	tgagtctccg	ctttgtggcc	acatgggtgtc	180
agatcaatat	gagcagctgt	cctctgaagc	cctgnganct	gcccgaaattt	gtgcccaataa	240
gtacatggta	aaaagtngtg	gonaagatgc	ttccatatcc	gggtgcggnt	ccaccccttcc	300
cacgtcatcc	gcatacaaaa	gatgttgtcc	tgtgtcgggg	ctgacagcgt	cccaacaggcg	360
atgcgaagtg	cctttggaaa	accganggca	ctgtggccag	ggttcacatt	ggggcaattn	420

atcatgttca tccgcaccaa ctgcagaaca angaactgt naattnaagc cctgcccagg 480
 gnaaanttca aatttcccgg cc 502

<210> 54
 <211> 494
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 431, 442, 445
 <223> n = A,T,C or G

<400> 54
 actagtccaa gaaaaatag cttaatgtat attacaaagg ctttgtatat gttaacctgt 60
 tttaatgcca aaagtttgct ttgtccacaa tttccttaag acctcttcag aaagggattt 120
 gtttgcccta atgaatactg ttgggaaaaa acacagtata atgagtgtaaa agggcagaagg 180
 caagaaattt tcacatctta ggcactocaa gaagaatgag tatccacatt tagatggcac 240
 attatgagga cttaaatctt tccttaacaa caataatgtt tctttttttc tttatttcac 300
 atgattttcta agtataattt tcatgcagga cagtttttca accttgatgt acagtgtactg 360
 tgttaaaattt tttcttcagt ggcaacctct ataattctta aaatatgtgt agcatcttgt 420
 ctgttttgaa ngggcatatga cnatnaatct atcagatggg aaatcctgtt tccaagttag 480
 aaaaaaaaaa aaaa 494

<210> 55
 <211> 606
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 375, 395, 511, 542, 559, 569, 578, 581
 <223> n = A,T,C or G

<400> 55
 actagtaaaa agcagcattg ccaataatc octaatttto cactaaaaat ataatagaat 60
 gatgttaaagc tttttgaaaa gtttaggtta aacctactgt tgttagatta atgtatttgt 120
 tgcttccctt tatctggaat gtggcattag cttttttatt ttaacctctt ttaattctta 180
 ttcaattcca tgacttaagg ttggagagct aaacactggg atttttggat aacagactga 240
 cagttttgca taattataat cggcattgta catagaaaag atatgggtac ctttttgttaa 300
 atctgcactt tctaaatctc aaaaaaggga aatgaagtat aaatcaattt ttgtataatc 360
 tgtttgaac atganttta ttgtcttaatt attanggtt tgccttttct tgttagtctc 420
 ttggatcctt gtgtaaaact gttctcatta aacaccaaag agttaagtcc attctcttgt 480
 actagctaca aattccgttt catattctac ntaacaattt aaattaactg aaattttctt 540
 anattgtcta cttctgtctt ataaaaacna aacttgantt nccaaaaaaa aaaaaaaa 600
 aaaaaa 606

<210> 56
 <211> 183
 <212> DNA
 <213> Homo sapiens

<400> 56
 actagtatat ttaaaacttac aggccttattt gtaatgtaaa ccaccatttt aatgtactgt 60
 aattaaacatg gttataatca gtacaatctt tccctcattc catcacacaa ctttttttgt 120
 gtgtgataaa ctgatttttg ttgtcaataa aaccttgaaa aataaaaaaa aaaaaaaa 180
 aaa 183

<210> 57
 <211> 622
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 358, 368, 412, 414, 425, 430, 453, 455, 469, 475, 495, 499,
 529, 540, 564, 575, 590
 <223> n = A,T,C or G

<400> 57
 actagtcaact actgtcttct cttgttagct aatcaatcaa tattcttccc ttgctgtggt 60
 gcagctggaga gtgctgctgg gtgtacgctg cacctgcccc ctgagttggg gaaagaggat 120
 aatcagtgag cactgttctg ctgagagctc ctgacttacc ccaccacctc ggatccagga 180
 ctgggtcaaa gctgcatgaa accaggccct ggagcaacc tgggaatggc tggaggtggg 240
 agagaacctg acttctcttt cctctccct cctccaacat tactggaact ctatcctgtt 300
 agggatcttc tgagcttgtt tcctgtgtgg gtgggacaga agacaaagga gaaggggangg 360
 tctacaanaa gcagcccttc ttgtctctct ggggttaagt agcttgacct ananttcagt 420
 gaganaccan aagcctctga tttttaattt cctnaaatg tttgaagtnt atatntacat 480
 atatatattt ctttnaatnt ttgagttctt gatattgtct aaaatccant cctctgtccn 540
 gaaacctgaa ttaaaacat gaanaaaat gtttncctta aagatgttan taattaattg 600
 aaacttgaaa aaaaaaaaaa aa 622

<210> 58
 <211> 433
 <212> DNA
 <213> Homo sapiens

<400> 58
 gaacaaattc tgatttggtta tgtaccgtca aaagacttga agaaatttca tgattttgca 60
 gtgtggaagc gttgaaatt gaaagtact gcttttccac ttgctcatat agtaaaggga 120
 tcttttcagc tgccagtgtt gaataatgta tcattccagag tgatgtttac tgtgacagtc 180
 accagcttta agctgaacca ttttatgaat accaaataaa tagacctott gtactgaaaa 240
 catattttgt actttaatgc tgcgtgttgg atagaaatat ttttactggg tcttctgaaat 300
 tgacagttaa cctgtccatt atgaatggcc tactgtttcta ttattttgtt tgacttgaat 360
 ttatccacca aagacttcatt ttgtgtatca tcaataaagt tgtatgtttc aactgaaaaa 420
 aaaaaaaaaa aaa 433

<210> 59
 <211> 649
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 22, 190, 217, 430, 433, 484, 544, 550, 577, 583, 594
 <223> n = A,T,C or G

<400> 59
 actagttatt atctgacttt cnggttataa tcattctaat gagtgtgaag tagcctctgg 60
 tgtcaattgg atttgoattt cctgtagtag tgatgctatc aagcaccttt gctgggtgctg 120
 ttggccatat gtgtatgttc cctggagaag tgcctgtgct gaggcctggc ccacttttta 180
 attaggcgtn tgccttttta ttactgagtt gtaaganttc ttatatatt ctggattcta 240
 gacccttata agatacatgg ttgcaaaata tttctccca tctgtgtggg tgtgtttcca 300
 ctttatcgat aatgtcctta gacatataat aaatttgat tttaaaagt acttgatttg 360
 ggctgtgcga ggtgggctca cgttgtaat ccagcactt tgggagactg aggtgggtgg 420
 atcatatgan gangctagga gttcgaggtc agcctggcca gcatagcga aacttgtctc 480

```

tacnaaaaat acaaaaatta gtcaggcatg gtggtgcacg tctgtaatac cagcttctca 540
ggangctgan gcacaaggat cacttgaacc ccagaangaa gangttgcag tganctgaag 600
atcatgccag ggcaacaaaa atgagaactt gtttaaaaaa aaaaaaaaaa 649

```

```

<210> 60
<211> 423
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 209, 222, 277, 389, 398
<223> n = A,T,C or G

```

```

<400> 60
actagtccag gccttcacgt tcaactgacaa acatggggaa gtgtgccag ctggctggaa 60
acctggcagt gataccatca agcctgatgt ccaaaagagc aaagaatatt tctccaagca 120
gaagtgcagc ctgggcctgtt ttagtccag gctgcggtgg gcagccatga gaacaaaacc 180
tcttctgtat ttttttttcc cattagtana acacaagact cngattcagc cgaattgttg 240
tgtctacaaa ggcaggcgtt tctacacagg ggtgganaaa acagcctttc ttcccttggt 300
aggaatggcc tgagtgtgcg ttgtgggcag gctactggtt tgtatgatgt attagtagag 360
caaccattat atcttttgtt gttgtatna aacttganct gagaccttaa acaaaaaaaa 420
aaa 423

```

```

<210> 61
<211> 423
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 195, 285, 295, 329, 335, 340, 347, 367, 382, 383, 391, 396,
418
<223> n = A,T,C or G

```

```

<400> 61
cgggactgga atgtaaagtg aagttcggag ctctgagcac gggctcttcc cgcggggtcc 60
tccctcccca gaccocagag ggagaggccc accccgccca gccccgcccc agcccctgct 120
caggctctgag tatggctggg agtcgggggc cacaggccct tagctgtgct gctcaagaag 180
actgattcag ggtanctaca agtggccggg ccttgccctt gggattctac cctgttccct 240
atttggtgtt ggggtgcggg gtccctggcc cctttttcca cactnccctc ctccngacag 300
caacotccct tggggcaatt gggcctggnt ctcncccggn tggtgcnacc ctttgttggt 360
ttaaggngctt taaaaatggt annttttccc ntgcnggggt taaaaaagga aaaaactnaa 420
aaa 423

```

```

<210> 62
<211> 683
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 218, 291, 305, 411, 416, 441, 443, 453, 522, 523, 536, 542,
547, 566, 588, 592, 595, 603, 621, 628, 630, 632, 644, 645,
648, 655, 660, 672, 674, 676, 677, 683
<223> n = A,T,C or G

```

```

<400> 62

```

```

gctggagagg ggtacggact ttcttgaggt tgtccaggt tggaaatgaga ctgaactcaa 60
gaagagacc taagagactg ggaatgggt cctgccttca ggaaagtga agacgcttag 120
gctgtcaaca cttaaaggaa gtcccttga agcccagagt ggacagacta gaccatttga 180
ggggccact ggccatggtc cgtggacaag acattccngt ggccatggc acaccggggg 240
ggatcaaaat gtgtacttgt ggggtctcgc ccttgccea aacaaaacca ntcccactcc 300
tgtonttga ctcttctccc attccctcct ccccaaatgc acttcccctc ctccccttgc 360
ccctcctgtg tttttggaat tctgtttccc tcaaaattgt taatttttta ntttngacc 420
atgaacttat gtttgggggt nangttcccc ttnccaatgc atactaatat attaatgggt 480
atttatcttt gaaatatctt ttaatgaact tggaaaaaat tnttgaatt tcttcttctc 540
cnttttnttt ggggggggtg gggggnrtgg ttaaaatttt tttggaancc cnatnggaaa 600
tnttaacttg gggcccccct naaaaaantn anttocaatt cttnnatngc cccntttccn 660
ctaaaaaaa ananannaaa aan 683

```

```

<210> 63
<211> 731
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 237, 249, 263, 288, 312, 317, 323, 326, 337, 352, 362, 370,
377, 400, 411, 414, 434, 436, 446, 457, 473, 486, 497, 498,
502, 512, 531, 546, 554, 563, 565, 566, 588, 597, 608, 611,
613, 615, 627, 632, 640, 641, 644, 654, 660, 663, 665
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 671, 678, 692, 697, 698, 699, 704, 705, 712, 714, 717, 718,
719, 723, 725, 730, 731
<223> n = A,T,C or G

```

```

<400> 63
actagtcaata aagggtgtgc cgttcttcga cgtggcggtc ttggcgccac tgetcgaga 60
cccgccctgc gacctcaagg tcatccactt ggtgcgtgat cccgcgcggg tggcgagttc 120
acggatccgc tcgcgccacg gcctcatccg tgagagccta cagggtgtgc gcagccgaga 180
ccgcgagctc accgcatgcc ctctctggag gccgcggggc acaagcttgg ccgccanaaa 240
gaaggcgtna gggggccgca aantaccacg ctctggggcg cctgaactgt cctcttgcaa 300
taatatgtgt tnaaaanctg canaanagcc cctgcancce cctgaactgt gntgcagggc 360
cncttacctn gtttggntgc ggttacaaag aacctgtttn ggaaaaccct nccnaaaacc 420
ttccgggaaa attntncaaa tttttnttgg ggaattnttg ggtaaaaccce ccnaaaatgg 480
gaaaentttt tgccctnnaa antaaacat tngttccgg gggccccccc ncaaaaccct 540
ttttnttttt tttntgcccc cantnncccc ccggggcccc ttttttting ggaaaanccc 600
ccccctncc nanantttta aaaggggggg anaatttttn nttncccccg ggggnccccc 660
ggngntaaaa nggttttccc cccccgaggg gngggggnnc ctcnnaaacc cntntcnnaa 720
cncnttttn n 731

```

```

<210> 64
<211> 313
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 240
<223> n = A,T,C or G

```

```

<400> 64
actagttgtg caaacacga ctgaagaaag acgaaaagt ggaaataact tgcaacgtct 60

```

```

gttagagatg gttgctacac atgttggttc tgtagagaaa catcttgagg agcagattgc 120
taaagtgtgat agagaatatg aagaatgcat gtcagaagat ctctcgaaa atattaaaga 180
gattagagat aagtatgaga agaaagctac tctaattaag tcttctgagg aatgaagatn 240
aaatgttgat catgtatata tatccatagt gaataaaatt gtctcagtaa agttgtaaaa 300
aaaaaaaaa aaa 313

```

```

<210> 65
<211> 420
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 400, 402, 403, 404, 405, 406, 409, 411, 412, 414, 415, 416
<223> n = A,T,C or G

```

```

<400> 65
actagttccc tggcaggcaa gggcttccaa ctgaggcagt gcatgtgtgg cagagagagg 60
caggaaagctg gcagtggtcag cttctgtgtc tagggagggg tgtggctccc tcttccctg 120
tcctggaggtg tggaggggaag aatctaggcc ttgacttgcc ctctcgccac cttccctt 180
gtagatactg ccttaacact cctcctctc tcagctgtgg ctgccacca agccaggttt 240
ctcgtgtctc actaatttat ttccaggaaa ggtgtgtgga agacatgagc cgtgtataat 300
atttgtttta acattttcat tgcaagtatt gaccatcatc cttggttgtg tatcgtgtga 360
acacaaatta atgatattaa aaagcatcca aacaaagccn annnnnaana nnnnnngaa 420

```

```

<210> 66
<211> 676
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 328, 454, 505, 555, 586, 612, 636, 641
<223> n = A,T,C or G

```

```

<400> 66
actagtttcc tatgatcatt aaactcattc tcagggttaa gaaaggaatg taaattttctg 60
cotcaatttg tacttcatca ataagttttt gaagagtgcg gattttttagt caggttcttaa 120
aataaaactc acaaatctgg atgcatttct aaattctgca aatgttttctt ggggtgactt 180
aacaaggaaat aatccacaa tatacctagc tacctaatac atggagctgg ggctcaaccc 240
actgtttttta aggatttgcg cttacttgtg gctgaggaaa aataagtagt tccgagggaa 300
gtagttttta aatgtgagct tatagatnng aaacagaata tcaacttaat tatggaaatt 360
gttagaaacc tgttctcttg ttacttgaat ctgtattgca attactattg tactggatag 420
actccagccc attgcaaaagt ctcagatata ttanctgtgt agttgaattc cttggaaatt 480
ttttttaaga aaaaattgga gtttnaaaga aataaacccc ttgtttaaat gaagcttggc 540
tttttggtga aaanaatca tccgcaggg cttattgttt aaaaanggaa ttttaagcct 600
ccctggaaaa antgtttaat taaatgggga aaatgntggg naaaaattat cagttagggt 660
ttaaagggaa aacttta 676

```

```

<210> 67
<211> 620
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 419, 493, 519, 568, 605, 610

```

<223> n = A,T,C or G

<400> 67

```

caccattaaa gctgcttacc aagaacttcc ccagcathtt gacttcottg tttgtatagt 60
gaattgtgag cagggtgatag aagagccttt ctatgtgaac atacagataa tttgctgaat 120
acattccatt taatgaagggt gttacatctg ttacgaagct actaagaagg agcaagagca 180
taggggaaaa aaatctgatac agaacgcatac gtgccccctc tactacaaaa 240
agattgtagt gctgtggtgtg tttattccgt tgtgcagaaac ttgcaagctg agtcaactaa 300
cccaaaagaga ggaaattata ggttagttaa acattgtaac ccaggaagct aagtttaatt 360
cacctttgaa gtgttttgtt ttttattttt gggtttgtctg atttactttg ggggaaaaag 420
ctaaaaaaaa agggatatca atctctaatt cagtgcocac taaaagttgt ccctaaaaag 480
tctttactcg aanttatagg actttttaag ctccaggtnl tttgtctctc caaatttaacc 540
ttgcatgggc cccttaaaat tgttgaangg cattctctgc tctaagtttg gggaaaatto 600
cccccatttn aaaaatttga

```

<210> 68

<211> 551

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 286, 464, 480, 501, 502, 518, 528, 533, 536, 537, 538, 539, 540, 541, 543, 544, 545, 547, 548, 549

<223> n = A,T,C or G

<400> 68

```

actagtagct ggtacataat cactgaggag ctattttetta acatgctttt atagaccatg 60
ctaagtctag accagtatatt aagggtctaact ctcacacctc cttagctgtga agagtctggc 120
ttagaacaga cctctctgtg caataacttg tggccactgg aaatccctgg gccggcattt 180
gtattggggt tgcaatgact cccaagggtc aaaagagtta aaggcaagac tgggatttct 240
tctgagactg tgggtgaaact ccttccaagg ctgagggggt cagtangtgc tctgggaggg 300
actcgccacc actttgatat tcaacaagcc acttgaagcc caattataaa attgttattt 360
tacagctgat ggaactcaat ttgaacottc aaaactttgt tagtttatcc tattatattg 420
ttaaacctaa ttacatttgt ctagcatttg atttggttcc tgtngcatat gtttttttcn 480
cctatgtgct cccctccccn nnatcttaat ttaaacncca attttgcnat tcnccnnnnn 540
nannnnnnna a

```

<210> 69

<211> 396

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 235, 310, 323, 381

<223> n = A,T,C or G

<400> 69

```

cagaaatgga aagcagagtt ttcattttctg tttataaaag tctccaaaaca aaaaatggaaa 60
gcagagtttt cattaaatcc ttttaacctt tttttttctt ggtaatcccc tcaaaataaca 120
gtatgtggga tattgaatgt taaagggata tttttttcta ttttttttat aattgtacaa 180
aattaagcaa atgttaaaag ttttatatgc tttattaatg ttttcaaaaag gtatnataca 240
tgtgatacat tttttaagct tcagttgctt gtctttctgt actttctgtt atgggctttt 300
ggggagccan aaaccaatct acnatctctt tttgttttgc aggacatgca ataaaaatta 360
aaaaataaat aaaaactatt nagaaattga aaaaaa

```

<210> 70

<211> 536
 <212> DNA
 <213> Homo sapiens

 <220>
 <221> misc_feature
 <222> 388, 446, 455
 <223> n = A,T,C or G

<400> 70
 actagtgcac aagcaaatat aaacatcgaa aaggcggttc tcacgttagc tgaagatatt 60
 ctctgaaaga ccctgtgtaa agagcccaac agtgaaaatg tagatatcag cagttggagga 120
 ggcggtgacag cgtggaagag caaatgctgc tgagcattct cctgttccat cagttgccat 180
 ccactacccc gttttctctt cttgctgcaa aataaacacc tctgtccatt ttttaactcta 240
 aacagatatt ttgttttctt atcttaacta tccaagccac ctattttatt tgttctttca 300
 tctgtgactg cttgtgtgact ttatcataat ttcttccaaa caaaaaaatg tatagaaaaa 360
 tcatgtctgt gacttcattt ttaaatgnta cttgctcagc tcaactgcatt ttcagttggt 420
 ttatagtcca gtctttatca acattnaaac ctatngcaat catttcaaat ctattctgca 480
 aattgtataa gaataaaagt tagaatattaa caattaaaaa aaaaaaaa aaaaaa 536

<210> 71
 <211> 865
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 22, 35, 39, 56, 131, 138, 146, 183, 194, 197, 238, 269, 277,
 282, 297, 316, 331, 336, 340, 341, 346, 349, 370, 376, 381,
 382, 392, 396, 397, 401, 433, 444, 445, 454, 455, 469, 472,
 477, 480, 482, 489, 497, 499, 511, 522, 526, 527
 <223> n = A,T,C or G

<221> misc_feature
 <222> 545, 553, 556, 567, 574, 580, 610, 613, 634, 638, 639, 663,
 672, 689, 693, 694, 701, 704, 713, 723, 729, 732, 743, 744,
 749, 761, 765, 767, 769, 772, 774, 780, 783, 788, 792, 803,
 810, 824, 840, 848
 <223> n = A,T,C or G

<400> 71
 gacaaagcgt taggagaaga anagaggcag ggaanaactn ccaggcacga tggcnccttt 60
 ccacacagca accagcgccc ccacacagcc ccagggccg gacgacgaag actccatcct 120
 ggattaatct naectctntc gcttgnccca ttctactctc ggaggtggag gccgggaaag 180
 tcncccaaag aganaanctg ctgccaaacac caacgcgcgc agccctggcg gccacganag 240
 gaaactggtg accaatctgc agaattctna gaggaaanaag cnagggggccc cgcgctnaga 300
 cagagctgga tatgangcca gacctggac nctacnccn ncaatncana cgggaactgcg 360
 gaagatggan gaccnccgac nngatcaggc cngctnncca nccccccacc cctatgaatt 420
 attcccgctg aangaatctc tgannggctt ccannaaagc gcctcccncc cnaacgnaan 480
 tncacactng ggattanang ctgggaactg naaggggcaa anoctnnaat attccccagaa 540
 acaanctctc ccnaanaaac tggggcncct catnggtggn accaactatt aactaaaccg 600
 cagcgccaagn aantataaaa gggggggccc tcncnngnng accocctttt gtcccttaatt 660
 ganggttatc cnccttgctt accatgggtnc ccnnttctgt ntgnatgttt cncctcccc 720
 cncctatnt cnagccgaac tcnatttnc ccgggggtgc nctcnantng tncnctttt 780
 ttngttgnc cngcccttcc cngcgggaac cgtttccccg ttantaacgg caccgggggn 840
 aagggtgntt ggcctccctc ctccc 865

<210> 72


```

<211> 560
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 83, 173, 183, 186, 209, 211, 215, 255, 321, 322, 323, 335,
344, 357, 361, 368, 394, 412, 415, 442, 455, 469, 472, 475,
487, 513, 522, 528, 531, 534, 546
<223> n = A,T,C or G

<400> 72
cctggacttg tcttggttcc agaacctgac gaccggcgga cgccgacgtc tcttttgact 60
aaaagacagt gtccagtgct cncgcctagg agtctacggg gaccgcctcc cgcgcgcgcca 120
ccatgcccaa cttctctggc aactggaaaa tcatccggtc ggaaaacttc gangaattgc 180
tcnaantgct gggggtgaat gtgatgctna ngaanattgc tgtggctgca gcgtccaagc 240
cagcagtgga gatcnaacag gaggggagaca ctttctacat caaaaactcc accaccgtgc 300
gcaccacaaa gattaacttc nnngttgggg agganittga ggancaaact gtggatngga 360
ngcctgtnaa aacctgtgtg aatggggagaa tganaataaa atggctctgt ancanaaact 420
cctgaaagga gaaggccccc anaactcctg gaccngaaaa actgaccncn cnatngggga 480
actgatnctt gaacctctga cggcggggat ganccttttt tnttgcncnc naanggggtc 540
tttctntttc cccaaaaaaa
560

<210> 73
<211> 379
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 8, 17, 18, 21, 26, 29, 30, 32, 53, 56, 67, 71, 81, 102, 104,
111, 112, 114, 119, 122, 124, 125, 134, 144, 146, 189, 190,
214, 215, 219, 220, 235, 237, 246, 280, 288, 302, 310, 313,
319, 322, 343, 353, 354
<223> n = A,T,C or G

<400> 73
ctggggganc ggcggtnnng nccatntcnn gncgcgaagg tggcaataaa aanccnctga 60
aaccgcncaa naaacatgcc naagatatgg acgaggaaga tngngctttc nngnacaanc 120
gnannagaga acanaacaaa ctcnangagc tctcaagcta atgccgcggg gaaggggccc 180
ttggccacnn gtggaattaa gaaatctggc aaanngtann tgttccttgt gcctnangag 240
ataagnagacc ctttatttca tctgtattta aacctctctn ttccctgncn taacttcttt 300
tnccacgtan agntggaant antgtgtgtc ttggactgtt gtnccatttta gannaaactt 360
ttgttcaaaa aaaaaataa
379

<210> 74
<211> 437
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 145, 355
<223> n = A,T,C or G

<400> 74
actagtgtcag actgccacgc caaccccaga aaatacccga catgccagaa aagtgaagtc 60
ctaggtgttt ccactatgt ttcaatctgt ccactaccca ggccctgcga taaaaacaaa 120

```

```

acaaaaaac gctgccaggt ttanaagca gttctggtct caaaaccatc aggatcctgc 180
caccagggtt cttttgaaat agtaccacat gtaaaaggga atttggtctt cacttcacat 240
aatcactgaa ttgtcagggt ttgattgata attgtagaaa taagtagcct tctgttggtg 300
gaataagtta taatcagtat tcatctcttt gttttttgtc actctttctt cctctnattgt 360
gtcatcttga ctggttgaaa aatatttctt ctataaaatt aaactaacct gccttaaaaa 420
aaaaaaaaa aaaaaaa

```

```

<210> 75
<211> 579
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 440, 513, 539, 551
<223> n = A,T,C or G

```

```

<400> 75
ctccgtgcgc gccagatga tgtgcggggc gccctccgcc acgcagccgg ccaccgcga 60
gaccagacac atcgccgacc aggtgaggtc ccagcttgaa gagaaagaaa acaagaagtt 120
ccctgtgttt aaggccgtgt cattcaagag ccaggttggtc gcgggggacaa actacttcat 180
caaggtgcac gtcggcgacg aggaactcgt acacotgcga gtgttccaat ctctccctca 240
tgaaaaacaag ccccttgacct tatctaaacta ccagaccaac aaagccaagc atgatgagct 300
gaacctattc tgatcctgac ttgggacaag gcccttcagc cagaagactg acaaaagtc 360
cctccgtcta ccagagcgtg cactttgatc cctaaaaataa gcttcacatc cgggctgtgc 420
ccttggggtg gaaggggcan gatctgcact gcttttgcat ttctcttctt aaatttcatt 480
gtgttgattc tttcctcca ataggtgatc tttnattactt tcagaatatt ttccaaatna 540
gatatatttt naaaatcctt aaaaaaaaaa aaaaaaaaaa

```

```

<210> 76
<211> 666
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 411, 470, 476, 491, 506, 527, 560, 570, 632, 636, 643, 650,
654, 658
<223> n = A,T,C or G

```

```

<400> 76
gtttatcccta tctctccaac cagattgtca gctccttgag ggcaagagcc acagtatat 60
tcctgttttc ttccacagtg cctaataata ctgtggaact aggttttaata aatttttta 120
ttgatgttgt tatgggcagg atggcaacca gaccattgtc tcagagcagg tgctggctct 180
ttcctggcta ctcaatgttg gctagcctct ggtaacctct tacttattat cttcaggaca 240
ctcaactacag ggaccaggga tgatgcaaca tccttgtctt tttatgacag gatgtttgct 300
cagctctctcc aacaataaaa agcacgtggg aaaaacacttg cggaattctt ggaactgttt 360
taaaaaatat acagtttacc gaaaatcata ttatcttaca atgaaaaagg ntttatagat 420
cagccagtga acaacctttt occaccatac aaaaattcct tttccogaan gaanaaggct 480
ttctcaataa noctcaattt cttaanatct tacaagatag ccccganact ttatcgaaac 540
tcatttttag caaatatgan ttttatgttn cgttacttgt ttcaaaattt ggtatttgtga 600
atatcaatta ccaccccat ctcccatgaa anaaanggga aanggtgaan ttcntaanag 660
cttaaa

```

```

<210> 77
<211> 396
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 31, 54, 125, 128, 136, 163, 168, 198
<223> n = A,T,C or G

<400> 77
ctgcagcccg ggggatccac taatctacca nggttatattg gcagctaatt ctanatttgg 60
atcattgccc aaagttgcac ttgctgggtct ctgggattt ggcccttgaa aggtatcata 120
catanganta tgcanaata aattccattt ttttgaanaa canctccnct gggctgtgtt 180
tggctccacag cataacangc actgcctcct tacctgtgag gaatgcacaaa taaagcatgg 240
attaagttag aagggagact ctacgacctc agcttccata attctgtgtc tgtgacttct 300
gaagtgtttt aaacctctga atttgtacac atttaaaatt tcaagtgtac tttaaaataa 360
aatacttota atgggaacaa aaaaaaaaaa aaaaaa 396

<210> 78
<211> 793
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 309, 492, 563, 657, 660, 703, 708, 710, 711, 732, 740, 748,
758, 762, 765, 787
<223> n = A,T,C or G

<400> 78
gcatcctagc cgccgactca cacaaggcag gtgggtgagg aaatccagag ttgccatgga 60
gaaaaatcca gtgtcagcat tcttgctcct tgtggccctc tctacactc tggccagaga 120
taccacagtc aaacctggag ccaaaaaagg cacaaggac tctogaccca aactgcccc 180
gacctctccc agaggttggg gtgaccaact catctggact cagacatatg aagaagctct 240
atataaatcc aagacaagca acaaacacct gatgattatt catcacttgg atgagtgtcc 300
acacagctcna gctttaaaga aagtgtttgc tgaaaaataa gaaatccaga aattggcaga 360
gcagttttgc ctctcaatc tggtttatga aacaactgac aaacacctt ctctgatgg 420
ccagtatgtc ccaggattat gtttgttgac ccattctctga cagttgaagc cgatatcctg 480
ggaagatatt cnaaccgtct ctatgcttac aaactgcaga tacgctctgt tgccttgacac 540
atgaaaaagc tctcaagttg ctnaaaatga attgtaagaa aaaaaatctc cagcctctctg 600
tctgtcggtg tgaaaaatga aaccagaaaa atgtgaaaaa tggctattgt ggaacanatn 660
gacacctgat taggttttgg ttatgttcac cactattttt aanaaaaan nttttaaaat 720
ttggttcaat tntcttttn aaacaatntg ttctacntt gngantctgat ttctaaaaaa 780
aataatnttt ggc 793

<210> 79
<211> 456
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 89, 195, 255, 263, 266, 286, 353, 384, 423, 425, 436, 441
<223> n = A,T,C or G

<400> 79
actagtatgg ggtgggaggg cccacacctc tccctaggc gctgttcttg ctccaaaggg 60
ctccgtggag agggactggc agagctgang ccacctgggg ctggggatcc caacttcttt 120
gcagctgttg agcgacacct accactggct atgccccacc cctgctctc cgcaccgcgt 180
tctctccgac cccangacca ggctacttct cccctctctc tgctctctc ctgcccctcg 240
tgctctctga cgtangaatt gangantgtc ccgcttctgt gctganaaat gacagtggca 300

```

```

ggggctggaa atgggtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt gcnccccc 360
tgcaagaccg agattgagg aaancatgtc tgctgggtgt gaccatgttt cctctccata 420
aantnccctc gtgacnctca naaaaaaaaa aaaaaa 456

```

```

<210> 80
<211> 284
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 283
<223> n = A,T,C or G

```

```

<400> 80
ctttgtacct ctgaaaaaga taggtattgt gtcatagaac ttgagtttaa attttatata 60
taaaactaaa agtaatgtct acttttagcaa cacatactaa aattggaacc atactgagaa 120
gaatagcatg acctccgtgc aaacaggaca agcaaatgtt tgatgtgttg attaaaaaga 180
aataataaaa tgtgtatatg tgtaacttgt atgtttatgt ggaatacaga ttgggaaata 240
aaatgtattt cttactgtga aaaaaaaaaa aaaaaaaaaa aana 284

```

```

<210> 81
<211> 671
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 388, 505, 600, 603, 615, 642, 644, 660
<223> n = A,T,C or G

```

```

<400> 81
gccaccaaca ttccaagcta cctgggttac ctttgtgcag tagaagctag tgagcatgtg 60
agcaagcggt gtgcacacgg agactcatcg ttataattta ctatctgccca agagttagaaa 120
gaaaggctgg ggatatttgg gttggcttgg ttttgatttt ttgctgtgtt gtttgttttg 180
tactaaaaca gtattatctt ttgaatatcg tagggacata agtatataca ttttatcoaa 240
tcaagatggc tagaatgttg cctttctgag tgtctaaaaac ttgacacccc tggtaaatct 300
ttcaacacac ttccaactgcc tgcgtaatga agttttgatc catttttaac caactggaatt 360
tttcaatgcc gtcatittca gttagatnat ttgacacttt gagattaaaa tggcatgtct 420
atttgattag tcttattttt ttatittttac aggcattatca gtctcactgt tggctgtcat 480
tgtgacaaa tcataataaac cccnaggac aacacacagt atgggatcac atattgtttg 540
acattaagct ttggccaaaa aatgttgcat gtgtttttacc tcgacttgct aaatcaatan 600
cnaaaaggct ggctnataat gtgggtgggt aaataattaa tnantaacca aaaaaaaaaa 660
aaaaaaaaa a 671

```

```

<210> 82
<211> 217
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 35
<223> n = A,T,C or G

```

```

<400> 82
ctgcagatgt ttcttgaatg ctttgtcaaa ttaanaaagt taaagtgc aa taatgtttga 60
agacaataag tgggtggtga tctgttttct aataagataa acttttttgt ctttgtctta 120

```

tottattagg gagttgtatg tcagtgatata aaacatactg tgtggtataa caggcttaat 180
 aaattcttta aaaggaaaaa aaaaaaaaaa aaaaaa 217

<210> 83
 <211> 460
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 104, 118, 172, 401, 422, 423, 444, 449
 <223> n = A,T,C or G

<400> 83
 cgcgagtgagg agcaccagga tctcgggctc ggaacgagac tgcacggatt gttttaagaa 60
 aatggcagac aaaccagaca tgggggaaat cgccagcttc gatnaggcca agctgaanaa 120
 aacggagacg caggagaaga acaccctgcc gaccaaaagag accattgagc angagaagcg 180
 gagtgaattt tcttaagatc ctggaggatt tcttaccctc gtcctcttcg agacccagct 240
 cgtgatgtgg aggaagagcc acctgcaaga tggacacgag ccacaagctg cactgtgaac 300
 ctggcgactc cgcgcgatg ccaccggcct gtgggtctct gaagggaccc cccccaatcg 360
 gactgccaaa ttctccggtt tgccccggga tattatacaa nattatttgt atgaataatg 420
 annataaaac acacctctgt gcancaana aaaaaaaaaa 460

<210> 84
 <211> 323
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 70, 138, 178, 197, 228, 242, 244, 287, 311
 <223> n = A,T,C or G

<400> 84
 tgggtgatct tggctctgtg gagctgctgg gacgggatct aaaagactat tctggaagct 60
 gtgggtccaan gcattttgct ggcttaacgg gtcccggaac aaaggacacc agctctctaa 120
 aattgaagtt taccoganat aacaatcttt tgggcagaga tgcctatttt aacaaacncc 180
 gtccctcgcc aacaacnaac aatctctggg aaataccggc catgaacnct ctgtctcaat 240
 cnancatctc tctagctgac cgatcataat gtcccagatt actacanatc ataataattg 300
 atttctctga naaaaaaaaa aaa 323

<210> 85
 <211> 771
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 63, 426, 471, 497, 521, 554, 583, 586, 606, 609, 615, 652,
 686, 691, 694, 695, 706, 713, 730, 732, 743, 751
 <223> n = A,T,C or G

<400> 85
 aaactgggta ctcaacactg agcagatctg ttcttttgagc taaaaacatc gtgctgtacc 60
 aanagtttgc tctcggctgc ttgatgtca gtgctgtac tcacacctctg cggcgaaatca 120
 gaagcaagca actttgactg ctgtcttggg tacacagacc gtattcttca tcttaaat 180
 attgtgggct tcacacggca gctggccaat gaaggctgtg acatcaatgc tatcatctt 240
 cacacaaaga aaaagtgtgc tgtgtgcgca aatccaaac agacttgggt gaaatatatt 300

```

gtgcgtctcc tcagtaaaaa agtcaagaac atgtaaaaac tgtggccttt ctggaatgga 360
attggacata gcccaagaac agaaagaact tgctgggggtt ggaggtttca ctgacacac 420
atgganggtt tagtgcttat cttattttgt cctcctggac ttgtccaatt natgaagtta 480
atcatattgc atcatanitt gctttgttta acatcacatt naaattaac tnatatttat 540
gttatttata gctntaggtt ttctgtgttt aactttttat acnaantttc ctataactatt 600
ttggtntant gcaanttaaa aattatattt ggggggggaa taaatattgg antttctgca 660
gccacaagct ttttttaaaa aaccantaca nccnngttaa atggtnngtc cnaatgggt 720
tttgcttttn antagaaaaa ttnttagaac natttgaaaa aaaaaaaaaa a 771

```

<210> 86

<211> 628

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 162, 249, 266, 348, 407, 427, 488, 518, 545, 566, 569, 597, 598, 611, 617, 621, 624

<223> n = A,T,C or G

<400> 86

```

actagtttgc tttacatttt tgaagaatgata tttttttgtc caagtgtcta tcaactaaac 60
cttgggttag gtaagaatgg aatttatttaa gtgaatcagt gtgaccttc ttgtcataag 120
attatcttaa agctgaagcc aaaatatgct tcaaaagaaa angactttat tttcattgt 180
agtccaatac ttcaagcat ctgaactgta gtttctatag caagccaatt acatccataa 240
gtggagaang aaatagatta atgtcnaagt atgattgggt gagggagcaa ggttgaagat 300
aatctgggggt tgaatttttc tagttttcat tctgtacatt tttagttna catcagatt 360
gaaattattaa tgtttaccct tcaatgtgtg gtatcagctg gactcantaa cacccttttc 420
ttccctnngg gatggggaat ggattattgg aaaaatggaa gaaaaagta cttaaagcct 480
tcctttcnca gtttctggct cctaccctac tgatttancc agaataagaa aacattttat 540
catntctgca tttattccca ttaatnaant tttgatgaat aaatctgctt ttatgcnnaa 600
ccaaggaatt nagtgmnto ntenttgt 628

```

<210> 87

<211> 518

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 384, 421, 486

<223> n = A,T,C or G

<400> 87

```

ttttttattt tttttagaga gtagttcagc ttttatttat aaatttattg cctgttttat 60
tataacaaca ttatactggt tagtggttaa tacatatggt tcaaaatgta taatacatca 120
agttagtcag ttttaaaatt ttatgcttaa aacaagtttt gtgtaaaaaa tgcagatcaa 180
ttttacatgg caaatcaatt ttttaagtcac cctaaaaatt gatTTTTTTT tgaattttaa 240
aaacacattt aatttcaatt tctctcttat ataaccttta ttactatagc atgggtttcaa 300
ctacagttta acaatgcagc aaaattccca ttccacggta aattgggttt taagcggcaa 360
ggtttaaagt ctttgaggat cctnaatacc ctttgaactt caaatgaagg ttatggttgt 420
naatttaacc ctcatgccat aagcagaagc acaagtttag ctgcattttg ctctaactctg 480
taaaanccag ccccccgttg aaaaagcaaa agggacc 518

```

<210> 88

<211> 1844

<212> DNA

<213> Homo sapiens

<400> 88

```

gagacagtg atcctagtagt caaaggattt ttggcctcag aaaaagtgtg tgattatttt 60
tatttttattt tatttttcga gactccgtct caaaaaaaa aaaaacacaa 120
ggtattttgct aaagcatttt gagctgcttg gaaaaagga agtagttgca gttagatttt 180
ttccatctctc ttgtgtcttg gaagccatct atgtgtcttt tactcaagct aaggggtata 240
agcttatgtg ttgaatttgc tacatctata ttccacatat tctcaacaata agagaatttt 300
gaatatagaaa tatcatagaa catttaagaa agtttagtat aaataatatt ttgtgtgttt 360
taatcccttt gaagggatct atccaaagaa aatatattac actgagctcc ttctacacag 420
tctcagtaac agatcccttg ttgtctttg aaaaatagctc atttttttaa tgcagtgag 480
tagatgtagc atacatatga tgtataatga cgtgtattat gttacaatg tctgcagatt 540
ttgtaggaa acaaaacatg gcctttttta taagcaaaa gggccaaatga ctgaaataac 600
acatagggca atctgtgaat atgtattata agcagcatto cagaaaagta gttggtgaaa 660
taattttcaa gtcaaaaagg gatattggaaa ggggaattat agtaacctct attttttaag 720
ccttgctttt aaattaaaag ctacagccat ttaagccttg aggataataa agcttgagag 780
taataatgtt aggttagcaa aggttttagat gtatcacttc atgcatgcta ccattgatagt 840
aatgcagctc ttctgagcat ttctggtcat tcaagatatt cacccttttg cccatagaaa 900
gcaccctacc tcacctgctt actgacattg tcttagctga tcacaagatc attatcagcc 960
tccatttatct ctactgtat ataaaatata gagttttata ttttcccttc ttctgttttt 1020
accatatatga aaacctaaat ttgtttttgc agatggaatg caaagtaac aagtgttgt 1080
gctttccactc agaaggggtg ggtcctgaag gaaagaggtc cctaataatc cccaccctgt 1140
ggtgtctctc ctccctgtgt accctgacta ccagaagtc ggtgtctgag cagctggaga 1200
agtgcagcag cctgtgcttc cacagatggg ggtgctgctg caacaggctc ttcaattgtc 1260
ccatcttagg gggagaagct agatcctgtg cagcagcctg gtaagtcctg agggagttcc 1320
atgtgctctc ctgctgctgt cctttgcttc tcaacggggc tcgctctaca gtctagagca 1380
catgcagcta actgtgctct ctgcttatgc atgagggtta aattacaacac cataaccttc 1440
atttgaagtt caaagtgcta ttcaggatcc tcaaacgatt taacctctgc cgtctaaaac 1500
ccaattttacc gtttaattgg aattttgtct cattgtttaa ctgtagtggg aaccattgta 1560
tagtaataaa ggttatataa gagagaaatt gaaattaaat gtttttttaa atttcaaaaa 1620
aaaaacaact tttaggatga cttaaaaatt gatttgcctt gtaaaatgta tctgcatttt 1680
ttacacaaaa cttgttttaa gcataaaatt ttaaaactgt actactgtat gttattaca 1740
ttttgaacca tatgtattaa accataaaca gtataatgtt gttataataa aacaggcaat 1800
aaattataa ataaaagctg aaaaaaaaaa aaaaaaaaaa aaaa 1844

```

<210> 89

<211> 523

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 288, 352, 369, 398, 475, 511, 513

<223> n = A,T,C or G

<400> 89

```

tttttttttt ttttttttag caatccacat ttattgatca cttattatgt accaggcact 60
gggataaaga tgactgtttag tcaactcagp taaggagaag aactagcaaa taagacgatt 120
acaattatgat tagagaaatg ctaagccaga gatatagaaa ggtcctattg ggtcctctg 180
tcaactgtgtc ttccacatc cctacccctc acaggccctc cctccagctg cctgcccccg 240
ctccccactc cagatccctt gggattttgc cttagagctaa acgaggganat gggccccctg 300
gcctctggcat gacttgaacc caaccacaga ctgggaaagg gagcctttgc anagtggtac 360
actttgatna gaaaacacat agggaaattg agagaaantc cccaatggc acccctgtct 420
ggtgtcctag aaaaagtttg agaattggata aatgaaggat caagggaatt aatanatgaa 480
taattgaatg gtggctcaat aagaatgact nontgtaagt acc 523

```

<210> 90

<211> 604

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 563

<223> n = A,T,C or G

<400> 90

```
ccagtggtggt ggaatgcaaa gattaccccg gaagctttcg agaagctggg attccctgca 60
gcaaaaggaaa tagccaatat gtgtcgtttc tatgaaatga agccagacgc agatgtcaat 120
ctacccaccac aactaaatcc caaagtcaaa agcttcagcc agtttatctc agagaaccag 180
gggagcctctc aagggcgatg agaaaatcag ctgttcagat aggcctctgc accacacagc 240
ctctttcctc ctctgatcct ttctcttcta cggcacaaca ttcatgtttg acagaacatg 300
ctggaatgca attgtttgca acaccgaagg atttctcgcg gtgcctctct cagtaggaag 360
cactgcattg gtgataggac agcgtaattt gattcacatt taacttgcta gttagtata 420
aggggtggta cacctgtttg gtaaaatgag aagcctcgga aacttgggag ctctctccct 480
accactaatg gggagggcag attattactg ggattttctc tggggtgaa taatttcaag 540
ccctaattgc tgaattccct ctnggcagcg tccagtttct tcaactgcac tgcaaaaatc 600
ccc
```

<210> 91

<211> 858

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 570, 591, 655, 664, 667, 683, 711, 759, 760, 765, 777, 787, 792, 794, 801, 804, 809, 817, 820

<223> n = A,T,C or G

<400> 91

```
tttttttttt ttttttttta tgattattat tttttttatt gatottttaca tcctcagttg 60
tgccagagatt tctgatgctt aataaacatt tgtttotgat agataagtgg aaaaaattgt 120
catttcctta ttcaagccat gcttttctgt gatattctga tcctagttag acatacagaa 180
ataaatgtct aaaaacagcac ctcgattctc gtctataaca ggactaagtt cactgtgatc 240
ttaataaagc ttggctaaaa tgggacatga gtggaggtag tcacacttca gcgaagaag 300
agaatctcct gtataatctc accaggagat tcaacgaatt ccaccacact ggactagtgg 360
atcccccggg ctgcaggaaat tggatatcaa gcttatcgat accgtcgacc tcgagggggg 420
gcccgggtacc caattcgccc tatagttagt cgtattacgc gcgctcactg gcgctcgttt 480
tacaacgtcg tgactgggaa aaccctggcg ttaccacact taatcgccct gcagcacatc 540
cccttttcgc cagctggcgt aatagcgaa agcccgacac gatcgccctt ncaacagtgg 600
cgcagcctga atggcgaaat ggacgcgccc tgtagcggcg cattaaagcg cggcnggggtg 660
tggnggntcc cccacgtgac cgnacacatt ggcagcgccct tacgcgcgtc ntctcgcttc 720
ttctcttctc ttctcgacac gttcgccggg ttcccccggn agctnttaat cgggggncct 780
cctttanggg tncnaattaa nggnttaacn gaccttngan cccaaaaact ttgattaggg 840
ggaaggtccc cgaagggg
```

<210> 92

<211> 585

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 317, 319, 320, 321, 325, 327, 328, 330, 331, 332, 460, 462, 483, 485, 487, 523, 538, 566, 584

<223> n = A,T,C or G


```

<400> 92
gttgaatctc ctggtgagat tatacaggag attctcttctc ttcgetgaag tgtgactacc 60
tccactcatg tccatttita gccaaagctta tttaagatca cagtgaactt agtctctgta 120
tagacgagaa tcgaggtgct gtttttagaca tttatttctg tatgttcaac taggatcaga 180
atatcacaga aaagcatggc ttgaataagg aaatgacaat tttttccact tatctgatca 240
gaacaaatgt ttattaaaga tcagaaactc tgccaacact gaggatgtaa agatcaataa 300
aaaaaataat aatcatnann naaanannan nngaaggcgc gccgccaccg cgggtggagct 360
ccagcttttg ttccctttag tgagggttaa ttgcgcgctt ggcggttaac atgggtcatag 420
ctgtttctctg tgtgaaattg ttatccggct cacaattccn cnaacatcac gagccgggaa 480
gcntnangtg taaaagcctg ggggtgccta attgagtgag ctnaactcaca ttaattngnt 540
tgcgtccac ttgcccgctt ttccantcog ggaacactgt tcgnc 585

```

```

<210> 93
<211> 567
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 82, 158, 230, 232, 253, 266, 267, 268, 269, 270, 271, 272,
273, 274, 275, 276, 277, 278, 279, 280, 281, 282, 283, 284,
285, 286, 287, 295, 303, 307, 314, 349, 352, 354, 356, 366,
369, 379, 382, 386, 393, 404, 427, 428, 446, 450, 452
<223> n = A,T,C or G

```

```

<221> misc_feature
<222> 453, 454, 459, 462, 480, 481, 483, 488, 493, 501, 509, 511,
512, 518, 520, 525, 526, 532, 541, 557
<223> n = A,T,C or G

```

```

<400> 93
cggcagtggt gctgtctgcg tgtccacott ggaatctggc tgaactggct gggaggacca 60
agactgcggc tgggggtggc anggaaggga accgggggct gctgtgaagg atcttggaac 120
ttccctgtac ccaccttccc ctgtgctcat gtttgtnanag gaaccttggt ccggccaagc 180
ccagtttctg tgtgtgatac actaatgtat ttgctttttt tgggaaatan anaaaaatca 240
attaaattgc tantgtttct ttgaannnnn nnnnnnnnnn nnnnnnnngg gggngcgcgc 300
cncnngngga aacnccccct ttgttccct ttaattgaaa ggtaattng cncncttggc 360
cttaancnct gggccaaanc tngttncocg tngtgaaatt gttnatcccc tcccaaatct 420
ccccccncc ttccaaaccc ggaanccctn annntgttna ancccggggg gttgcctaan 480
ngnaattnaa cnaaccccc ntttaaatng nntttgcncn ccacnngccc cnccttccca 540
nttcggggaa aacctntccc gtgccca 567

```

```

<210> 94
<211> 620
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 169, 171, 222, 472, 528, 559, 599
<223> n = A,T,C or G

```

```

<400> 94
actagtcaaa aatgctaaaa taatttggga gaaaatattt tttaagtagt gttatagttt 60
catgtttatc ttttattatg ttttgtgaag ttgtgtcttt tcactaatca cctatactat 120
gccaatattt ccttatatct attccataaca tttatatact atttgaana naatatgac 180
gtgaaactta acactttata aggtaaaaat gaggtttcca anatttaata atctgatcaa 240

```

```

gttcttgttta ttccaaata gaatggactt ggtctgttaa gggctaagga gaagaggaag 300
ataagggttaa aagtgtgttaa tgaccaaaca ttctaaaaga aatgcaaaaa aaaagtgttat 360
tttcaagcct togaactatt taaggaaagc aaatcattt cctaaatgca tatcatttgt 420
gagaatttct cattaatato ctgaatcatt catttacta aggcctatgt tnaactcogat 480
atgtctctaa gaaagtacta tttcatggtc caaacctggt tgccatantt gggtaaaggc 540
tttcccttaa gtgtgaaant atttaaaatg aaatttttct ctttttaaaa attctttana 600
agggttaaggt gtgtggggga

```

<210> 95

<211> 470

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 61, 67, 79, 89, 106, 213, 271, 281, 330, 354, 387, 432, 448

<223> n = A,T,C or G

<400> 95

```

ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
nactttntgc ttaattcang agcttacang attcttcaaa gagtgngtcc agcatccttt 120
gaaacatgag ttcttaccag cagaagcaga cctttacccc accacotcag cttcaacagc 180
agcaggtgaa acaaccctac cagcctccac ctgaggaat atttgttccc acaaccaagg 240
agccatgcca ctcaaagggt ccacaacctg naaacacaaa nattccagag ccaggctgta 300
ccaagggtcc tgagccaggg ctgtaccaan gtccctgagc cagggtgtac caangtccct 360
gagccaggat gtaccaagggt ccctgancca ggttgtccaa ggtccctgag ccaggctaca 420
ccaagggcct gngccaggca gcatacaangt ccttgaccaa ggcttatcaa 470

```

<210> 96

<211> 660

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 299, 311, 360, 426, 538, 540, 542, 553, 563, 565, 592, 603,

604, 618, 633, 647, 649, 651, 653

<223> n = A,T,C or G

<400> 96

```

tttttttttt tttttttttt ggaattaaaa gcaatttaaat gagggcagag caggaaacat 60
gaatttcttt tcattcgaat ctccagatga accctgagca gcggaagacc agaaaaacca 120
tgaagacttt ctgcttaatt cagggggctta caggattctt cagagtgtgt gtgaacaaaa 180
gctttatagt acgtattttt aggatacaaa taagagagag actatggcct ggggtgagaa 240
tgtactgatt acaagggtcta cagacaatta agacacagaa acagatggga agagggtgnc 300
cagcatctgg nggttggcct ctcaagggct tgtctgtgca ccaaatattc tctgcttgn 360
ctctctgtga gctgggcctg gagtgaacct tgaaggacat ggctctggta cctttgtgta 420
gcctgncaca ggaactttgg tgtatccttg ctacaggact ttgatggcac ctggctcagg 480
aaacttgatg aagccttggt caagggacct tgatgcttgc tggctcaggg accttggngn 540
ancctgggct canggacctt tgnncncaacc ttggcttcaa gggacccttg gnacatcctg 600
gcnnagggac ccttgggncc aaccctgggc tttagggacc ctttggntnc nanccctggc 660

```

<210> 97

<211> 441

<212> DNA

<213> Homo sapiens

```

<220>
<221> misc_feature
<222> 12, 308
<223> n = A,T,C or G

<400> 97
gggaccatac anagtattcc tctcttcaca ccaggaccag ccactgttgc agcatgagtt 60
cccagcagca gaagcagccc tgcattccac cccctcagct tcagcagcag caggtgaaac 120
agccttgcca gcctccacct caggaaacct gcattcccaa aaccaaggag ccttgccacc 180
ccaaggtgcc tgagccctgc caccaccaag tgccctgagcc ctgccagccc aaggttccag 240
agccatgcgc cccaaggtg cctgagccct gcccttcaat agtcaactcca gccacagccc 300
agcagaanac caagcagaag taatgtggtc cacagccatg cccttgagga gccggccacc 360
agatgctgaa tcccctatcc cattctgtgt atgagtccta ttgctctgc aattagcatt 420
ctgtctcccc caaaaaaaaa a                                     441

<210> 98
<211> 600
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 295, 349, 489, 496, 583
<223> n = A,T,C or G

<400> 98
gtattcctct cttcacacca ggaccagcca ctgttgagcg atgagttccc agcagcagaa 60
gcagccctgc atcccccccc ctgagcttca gcagcagcag gtgaaacagc cttgccagcc 120
tcacactcag gaaccatgca tccccaaaac caaggagccc tgccacccca aggtgctcga 180
gccttgccac cccaagtgcc ctgagccctg ccagcccaag gttccagagc catgccaccc 240
caaggtgcct gagccctgcc ctccaatagt cactccagca ccagcccagc agaanaacca 300
gcagaagtaa tgtgtgccac agccatgccc ttgaggagcc gccaccana tgctgaatcc 360
cctatcccat tctgtgtatg agtcccattt gccttgcaat tagcattctg tctcccccaa 420
aaaagaatgt gctatgaagc tttcttttct acacactctg agtctctgaa tgaagctgaa 480
ggtcttaant acagantcag ttttcagctg ctccagaattc tctgaagaaa agatttaaga 540
tgaaggcaa atgattcagc tccttattac cccattaaat tcnctttcaa tccaaaaaaa 600

<210> 99
<211> 667
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 345, 562, 635
<223> n = A,T,C or G

<400> 99
actagtgtact gagttcctgg caaagaaatt tgacctggac cagttgataa ctcatgtttt 60
accatttaaa aaaatcagtg aaggatttga gctgctcaat tcaggacaaa gcattcgaac 120
ggtcctgacg ttttgagatc caaagtgcca ggaggtctgt gttgtctatg tgaactggag 180
ttctctctgt gagagttccc tcatctgaaa tcatgtatct gtctcacaaa tacaagcata 240
agtgaagaag ttgttgaaga catagaaccc ttataaacct ttataaacat 300
ttaaagtctt gtgagcacct ggggaattagt ataatacaaa tgtttnatatt tttgatttac 360
attttgtaag gctataattg tatcttttaa gaaaacatac cttggatttc tatgttgaaa 420
tggagatttt taagagtttt aaccagctgc tgcagatata ttactcaaaa cagatatagc 480
gtataaagat atagtaaatg catctcctag agtaatatcc acttaacaca ttggaacta 540

```

```

ttatttttta gatttgaata tnaatgttat tttttaaaca cttgttatga gttacttggg 600
attacatttt gaaatcagtt cattccatga tgcanaattac tgggattaga ttaagaaaga 660
cggaaaaa 667

```

```

<210> 100
<211> 583
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 404, 506, 514, 527, 528, 538, 548, 556, 568, 569
<223> n = A,T,C or G

```

```

<400> 100
gttttggttg taagatgatc acagtcctgt tacactgatc taaaggacat atataatacc 60
ctttaaaaaa aaatcactcg cctcattctt atttcaagat gaatttctat acagactaga 120
tgttttttctg aagatcaatt agacattttg aaatgattt aaagtgtttt ccttaagtgt 180
ctctgaaaaac aagtttcttt ttgtagtttta accaaaaaag tgcctttttt gtccactggat 240
tctctagca ttcattgattt ttttttcata caatgaaatt aaaattgcta aaatcatgga 300
ctgggtttctt gggtggattt caggtaagat gtgtttaagg ccagagcttt tctcagtatt 360
tgattttttt ccccaatatt tgatttttta aaaatatata catnggtgct gcatttatat 420
ctgctgtttt aaaattctgt catatttcac ttctagcctt ttagtatatg caaatcatat 480
tttacttttta cttaaagcat ttggttattt ggantatctg gtctctannct aaaaaaanta 540
attctatnaa ttgaantttt ggtactcnnc catatttgga tcc 583

```

```

<210> 101
<211> 592
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 218, 497, 502, 533, 544, 546, 548, 550, 555
<223> n = A,T,C or G

```

```

<400> 101
gtggagacgt acaaagagca gccgctcaag acacctggga agaaaaagaa aggcgaagccc 60
gggaacgcga aggagcagga aaagaaaaaa oggcgaactc gctctgcctg gttagactct 120
ggagtgcactg ggaagtggct agaaggggac cactgtctcg acacctccac aacgcgcgtg 180
gagctcgatt caccgaggca ttgaaatttt cagcaganaac cttccaagga catattgcag 240
gattctgttaa tagtgaacat atggaagta ttagaataat ttattgtctg taaatactgt 300
aaatgcattg gaataaaaact gtctccoccca ttgctctatg aaactgcaca ttggtcattg 360
tgaattattt ttttttggcc aaggctaatc caattattat tatcacattt accataattt 420
attttgtcca ttgatgtatt tattttgtaa atgtatcttg gtgctgtcga atttctatat 480
tttttgtaca taatgcnttt anataacct atcaagtttg ttgataaatg aoncaatgaa 540
gtgnononan ttgngggttg aatttaatga atgctcaatt ttattatccc aa 592

```

```

<210> 102
<211> 587
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 91, 131, 256, 263, 332, 392, 400, 403, 461, 496, 497, 499,
510, 511, 518, 519, 539, 554, 560, 576
<223> n = A,T,C or G

```

```

<400> 102
cgctcctaagc acttagacta catcagggaag gaacacagac cacatccctg tcctcatgog 60
gcttatgttt tctggaagaa agtggagacc nagtccttgg ctttaggggt ccccgctgg 120
gggctgtgca ntccggtcag ggccgggaagg gaaatgcacc gctgcatgtg aaactacagc 180
ccaggcggat gccctctccc tttagcactac ctggccctct gcacccccct gcctcatgtt 240
ctccccacct tcaanaaatg aanaacccca tgggcccagc cccttgcctt ggggaaccaa 300
ggcagccttc caaaactcag gggctgaagc anaactattag ggcagggggt gactttgggt 360
gacactgccc attcctctc agggcagctc angtcacccn ggnotcttga acccagcctg 420
ttcctttgaa aaagggcaaa actgaaaagg gcttttccca naaaaagaaa aaccagggaa 480
ctttgccagg gcttcnntnt taccaaaaacn ncttctcnng gatttttaat tcccattng 540
gctccactt accnggggcn atgcccacaa attaanaatt tcccatc 587

```

```

<210> 103
<211> 496
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 2, 17, 66, 74, 82, 119, 164, 166, 172, 200, 203, 228, 232,
271, 273, 415, 423, 445, 446, 473
<223> n = A,T,C or G

```

```

<400> 103
anaggactgg cctcactnct tctctctcgt cctacactatc aatgcccac atggcgagaac 60
ctgcancctt tggncactgc anattggaac ctctcagttg ctgacacatc cctaccctt 120
ggggtgggtc tccacacaaa ccactttgac tctgtgttcc ctgnanggtg gnttctcctg 180
actggcgagg tggaccttan cncacatcct cctctgttcc ctctgctnag aaaaagaatt 240
cccttaacat gatataatcc acccatgcaa ntngctactg gcccgctac catttaacat 300
ttgctacag aatttcatc agtctacact ttggcattct ctctggcgat agagtgtggc 360
tggcgtagcc gcaaaagggt ccttacacac tggccccac cctcaaccgt tgacncatca 420
gangcttgcc tctcctctct gattnncccc catgttggat atcagggtgc tonaggatt 480
ggaaaaagaa caaaac 496

```

```

<210> 104
<211> 575
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 18, 19, 45, 68, 77, 132, 155, 174, 219, 226, 238, 259, 263,
271, 273, 306, 323, 339, 363, 368, 370, 378, 381, 382, 436,
440, 449, 450, 456, 481, 485, 496, 503, 510, 512, 515, 528,
542, 552
<223> n = A,T,C or G

```

```

<400> 104
gaacctctgc tcaatccnnc tctcaccatg atcctccgcc tgcanaaact cctctgccaa 60
ctatggangt ggtttcnngg gtggctcttg ccaactggga agaagccgtg gtgtctctac 120
ctgttcaact cngtttgtgt ctgggggcat aactnngggc tatggaagcg gctnaactgt 180
tgttttgtgt gaagggtcgt taattggcct tgggaagtng cttatngaat ttggccctng 240
gaagtgtcta ttgaaagtng ccttggaagt ngntttgtgt gggggttttg ctggtggcct 300
tgtttnaatt tgggtgcttt gtnaatggcg gcccccctnc ctgggcaatg aaaaaaatca 360
cnaatgcnng aaacctcnac nnaacagcct gggcttccct cacctcgaaa aaagtgtgct 420
cccccccaa aaaggncaan cccctcaann tggaaangtt aaaaaatcct cgaatgggga 480
nccnnaaaac aaaaancccc ccttttcccn gnaanggggg aaataccnc ccccaacta 540

```

```

cnaaaaccct tntaaaaaac cccccgggaa aaaa          575

<210> 105
<211> 619
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 260, 527, 560, 564, 566, 585, 599
<223> n = A,T,C or G

<400> 105
cactagtagg atagaaacac tgtgtccoga gagtaaggag agaagctact attgattaga 60
gcctaaaccca ggtaactgc aagaagaggc gggatacttt cagctttcca tgtaactgta 120
tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctaact gaatcccaact 180
tcaatacaca ctcatgaact cctgatggaa caataacagg cccaagcctg tgggtatgatg 240
tgcaacacttg ctgagactcan aaaaaatact actctcataa atgggtggga gtattttggt 300
gacaacctac tttgcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
gacattttagt tagtgctttt tatataccag gcatgatgct gagtgcacat cttgtgtata 420
tttccaaatt tttgtacagt cgctgcacat atttgaaatc atatattaa gactccaaaaa 480
aatgaagttc ctgggttttc atggcaactt gatcagtaaa ggattcncct ctgttttgga 540
cttaaaacat ctactatatn gtttnaatga aattcctttt cccnccctcc cgaaaaaana 600
aagtgggtgg gaaaaaaa

<210> 106
<211> 506
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 8, 21, 31, 32, 58, 75, 89, 96, 99, 103, 122, 126, 147, 150,
158, 195, 210, 212, 219, 226, 246, 248, 249, 255, 258, 261,
263, 265, 275, 304, 317, 321, 331, 337, 340, 358, 371, 377,
380, 396, 450, 491
<223> n = A,T,C or G

<400> 106
cattggtnct ttcatttgct ntggaagtgt nnatctctaa cagtggacaa agttcccngt 60
gccttaaaact ctgtnacact tttgggaant gaaaanttng tantatgata ggttattctg 120
angtanaagat gttctggata ccattanatn tgccccngt gtcagaggct catattgtgt 180
tatgtaaatg gtatntcatt cgctactatn antcaattng aaatanggtc tttgggttat 240
gaatantnng cagcncanct nanangctgt ctgtngtatt cattgtggtc atagcaacct 300
acancattgt aacctnctc nagtgagaca nactagnaan ttccatagta tggctcanga 360
ttccaaatgg nctcatntcn aatgttttaa agttanttaa gtgtaagaaa tacagactgt 420
atgttccacc aactagtacc tgtaatgacn ggccgtgtccc aacacatctc ccttttccat 480
gactgtggta nccgcgatcg gaaaaa          506

<210> 107
<211> 452
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 289, 317, 378
<223> n = A,T,C or G

```

```

<400> 107
gttgagctctg tactaaacag taagatatct caatgaacca taaattcaac ttgttaaaaa 60
tctttttgaag catagataat attgtttggt aaatgtttct ttgttttggg aaatgtttct 120
tttaagacc ctccattctc ataaactctc gcatgtagag gcttgtttac cttctctctc 180
ctaagggtta caataggagt ggtgatttga aaaatataaa attatgagat tggttttctc 240
gtggcataaaa ttgcatact gtatcatttt cttttttaac cggtaagant ttcaagttgt 300
tggaagtaa ctgtganaac ccagtttccc gtccatctcc cttagggact acccatagaa 360
catgaaaagg tcccacnga agcaagaaga taagtcttcc atgggtctgt gttgcttaaa 420
ccactttaaa accaaaaaa tccccttggg aa
452

<210> 108
<211> 502
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 22, 31, 126, 168, 183, 205, 219, 231, 236, 259, 283, 295,
296, 298, 301, 340, 354, 378, 383, 409, 433, 446, 455, 466,
488
<223> n = A,T,C or G

<400> 108
atctctctcc cttaattagt tnttatttat ntattaaatt ttattgcatg tctgtggcaa 60
caaaaagaga ttgtagattg gcttctggct ccccaaaagc ccataacaga aagtaccaca 120
agaccncaac tgaagcttaa aaaactctat acatgtataa taccttnga agaaccattaa 180
tanagcatat aaaactttta acatntgctt aatgttgnac aattataaaa ntaatngaaa 240
aaaatgtccc tttaacatnc aatatccac atagtgttat tttaggggat taccnngnaa 300
ncaaaaagg gtgagaagga ttaaatgaaa actctgcttn ccatttctgt ttanaaacgt 360
ctccagaaca aaaacttntc aantctttca gctaacocga tttagactna ggccactcaa 420
aaactccatt agnccactt tctaangtcc tctanagctt actaancctt ttgaccocct 480
accctgnta ctctgacct ca
502

<210> 109
<211> 1308
<212> DNA
<213> Homo sapiens

<400> 109
accggagctg tcgctaaaat catcatggat tcaacttggc cgtcagcac tgcacttggg 60
ttgtatcttt tcaaaagact gaagaaaaca aatgatggca acatctcttt ttccccgtgt 120
ggcatcttga ctgcaattgg catgttctct cttggggacc gaggagccac cgcttccacc 180
ttggaggagg tgtttcactc tgaaaaagag cagaagagct catcaacaa ttgactgtga 240
aaagagggtg ttgagaacac agaagcagta acataacaa tccaaaagtt ttgactgtga 300
ataagcaaac tcaactaatg ttatgaactg aacataacca acaggctgtt ttggagaaaa 360
acatacctct tccctcaaaa atacttagat tatgttgaaa aatattatca tgcactctctg 420
gaacctgtgt attttgtaaa tgcagccgat gaagctgcaa agaagattaa ttctgtgggt 480
gaagacaaaa caaatgaaaa aatcaaggac ttgttccag atggctctat tagtagctct 540
accaagctgg tgctgtgtga catgttttat tttaaagggc aatgggagac ggagtttaag 600
aaagaaaaata ctatgaaaga gaaatttttg atgaataaga gcacaagtaa atctgtacag 660
atgatgacac agagccattc ctttagcttc actttctctg aggactgtga gcccacaatt 720
ctagggtatc catataaaaa caacgacctc agcatgtttg tgctctgtcc caacgacctc 780
gatggcctgg agaagataat agataaaata agtctctgaa aattgtgtga gtggactagt 840
ccagggcata tgggaagaaag aaagtgtaac ctgcacttgc ccggttttga ggtggaggac 900
agttacgata tagaggcggt cctggctgcc atggggatgg gcgatgcctt cagtgtgacac 960
aaagccgact actcgggaat gtgcctcaggc tccgggttgt acgcccagac gttcctgcac 1020
agttccctttg tggcagtaac tgaggaaggg accgagctgt cagctgcacac tggcagtagc 1080

```

```

tttactgtca catccgcccc aggtcatgaa aatgttcaat gcaatcatcc ctctcgtgtc 1140
ttcatcaaggc acaatgaatc caacagcatc ctcttcttcg gcagattttc ttctccttaa 1200
gatgatcgtt gccatggcat tgctgctttt agcaaaaaac aactaccagt gttactcata 1260
tgattatgaa aatcgtccat tcttttaaat ggtggctcac ttgcattt 1308

```

<210> 110
 <211> 391
 <212> PAT
 <213> Homo sapiens

<400> 110
 Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
 1 5 10 15
 Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
 20 25 30
 Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
 35 40 45
 Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
 50 55 60
 Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Ile Glu Asn Thr Glu
 65 70 75 80
 Ala Val His Gln Gln Phe Gln Lys Phe Leu Thr Glu Ile Ser Lys Leu
 85 90 95
 Thr Asn Asp Tyr Glu Leu Asn Ile Thr Asn Arg Leu Phe Gly Glu Lys
 100 105 110
 Thr Tyr Leu Phe Leu Gln Lys Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr
 115 120 125
 His Ala Ser Leu Glu Pro Val Asp Phe Val Asn Ala Ala Asp Glu Ser
 130 135 140
 Arg Lys Lys Ile Asn Ser Trp Val Glu Ser Lys Thr Asn Glu Lys Ile
 145 150 155 160
 Lys Asp Leu Phe Pro Asp Gly Ser Ile Ser Ser Ser Thr Lys Leu Val
 165 170 175
 Leu Val Asn Met Val Tyr Phe Lys Gly Gln Trp Asp Arg Glu Phe Lys
 180 185 190
 Lys Glu Asn Thr Lys Glu Glu Lys Phe Trp Met Asn Lys Ser Thr Ser
 195 200 205
 Lys Ser Val Gln Met Met Thr Gln Ser His Ser Phe Ser Phe Thr Phe
 210 215 220
 Leu Glu Asp Leu Gln Ala Lys Ile Leu Gly Ile Pro Tyr Lys Asn Asn
 225 230 235 240
 Asp Leu Ser Met Phe Val Leu Leu Pro Asn Asp Ile Asp Gly Leu Glu
 245 250 255
 Lys Ile Ile Asp Lys Ile Ser Pro Glu Lys Leu Val Glu Trp Thr Ser
 260 265 270
 Pro Gly His Met Glu Glu Arg Lys Val Asn Leu His Leu Pro Arg Phe
 275 280 285
 Glu Val Glu Asp Ser Tyr Asp Leu Glu Ala Val Leu Ala Ala Met Gly
 290 295 300
 Met Gly Asp Ala Phe Ser Glu His Lys Ala Asp Tyr Ser Gly Met Ser
 305 310 315 320
 Ser Gly Ser Gly Leu Tyr Ala Gln Lys Phe Leu His Ser Ser Phe Val
 325 330 335
 Ala Val Thr Glu Glu Gly Thr Glu Ala Ala Ala Thr Gly Ile Gly
 340 345 350
 Phe Thr Val Thr Ser Ala Pro Gly His Glu Asn Val His Cys Asn His
 355 360 365
 Pro Phe Leu Phe Phe Ile Arg His Asn Glu Ser Asn Ser Ile Leu Phe

370
Phe Gly Arg Phe Ser Ser Pro
385 390

380

<210> 111
<211> 1419
<212> DNA
<213> Homo sapiens

<400> 111
ggagaactat aaattaagga tcccagctac ttaattgact tatgcttctt agttcgttgc 60
ccagccaccca ccgtctctcc aaaaaccgga ggtctcgcta aaatcatcat ggattcaactt 120
ggcgccgcga gcactcgact tgggtttgat cttttcaaa agctgaagaa aacaaatgat 180
ggcaacatct tcttttcccc ttgtgggcac ttgactgcaa ttggcatggt cctcctgggg 240
acccgaggag ccaccgcttc ccagttggag gaggtgttct actctgaaaa agagacgaag 300
agctcaagaa taaaggctga agaaaaagag gtggtaagaa taaaggctga aggaaagag 360
attgagaaca cagaagcagt acatcaacaa ttccaaaagt ttttgactga aataagcaaa 420
ctcactaatg attatgaact gaacataacc aacaggctgt ttggagaaaa aacatacctc 480
ttccttcaaa aatacttaga ttatgttgaa aaatattatc atgcattctct ggaacctgtt 540
gatttttgtaa atgcagccga tgaagtcga aagaagatta attcctgggt tgaagcaaa 600
acaaatgaaa aaatcaagga cttgttccca gatggctcta ttagtagctc taccaagctg 660
gtgctgtgga acatgggtta ttttaaaagg caatgggaca gggagttaa gaaagaaat 720
actaaggaag agaaattttg gatgaataag agcacaagta aatctgtaca gatgatgaca 780
cagagccatt ccttttagctt cactttctct gaggacttgc aggccaaaaa tctagggatt 840
ccatataaaa caacagacct aagcatgttt gtgcttctgc ccaacgacat cgatggcctg 900
gagaagataa tagataaaat aagtcctgag aaattggtag agtggaactag tccagggcac 960
atggagaaga gaaagggtgaa tctgcaactt ccccggtttg aggtggagga cagttagcat 1020
ctagaggcgg tctcggtcgc catggggatg ggcgatgctc tcaagtgaaga caaagccgac 1080
tactcggaag ttgctgcagg ctccgggttg tacgccaga agttctcgca cagttccttt 1140
gtggcagtaa ctgaggaagg caccgaggtc gcagctgcca ctggcatagg ctttactgtc 1200
acatccgccc caggctcatg aaatgttccac tgcattcatc ccttctgttt ctctcatcag 1260
cacaatgaat ccaacagcat cctcttcttc ggcagatttt cttctctcta agatgatcgt 1320
tgccatggca ttgctgcttt tagcaaaaaa caactacag tgttactcat atgattatga 1380
aaatgctcca ttcttttaaa tgggtgctca cttgcattt 1419

<210> 112
<211> 400
<212> PRT
<213> Homo sapiens

<400> 112
Met Asp Ser Leu Gly Ala Val Ser Thr Arg Leu Gly Phe Asp Leu Phe
1 5 10 15
Lys Glu Leu Lys Lys Thr Asn Asp Gly Asn Ile Phe Phe Ser Pro Val
20 25 30
Gly Ile Leu Thr Ala Ile Gly Met Val Leu Leu Gly Thr Arg Gly Ala
35 40 45
Thr Ala Ser Gln Leu Glu Glu Val Phe His Ser Glu Lys Glu Thr Lys
50 55 60
Ser Ser Arg Ile Lys Ala Glu Glu Lys Glu Val Val Arg Ile Lys Ala
65 70 75 80
Glu Gly Lys Glu Ile Glu Asn Thr Glu Ala Val His Gln Gln Phe Gln
85 90 95
Lys Phe Leu Thr Glu Ile Ser Lys Leu Thr Asn Asp Tyr Glu Leu Asn
100 105 110
Ile Thr Asn Arg Lys Glu Phe Gly Glu Lys Thr Tyr Leu Phe Leu Gln Lys
115 120 125

Tyr Leu Asp Tyr Val Glu Lys Tyr Tyr His Ala Ser Leu Glu Pro Val
 130 135 140
 Asp Phe Val Asn Ala Ala Asp Glu Ser Arg Lys Lys Ile Asn Ser Trp
 145 150 160
 Val Glu Ser Lys Thr Asn Glu Lys Ile Lys Asp Leu Phe Pro Asp Gly
 165 170 175
 Ser Ile Ser Ser Ser Thr Lys Leu Val Leu Val Asn Met Val Tyr Phe
 180 185 190
 Lys Gly Gln Trp Asp Arg Glu Phe Lys Lys Glu Asn Thr Lys Glu Glu
 195 200 205
 Lys Phe Trp Met Asn Lys Ser Thr Ser Lys Ser Val Gln Met Met Thr
 210 215 220
 Gln Ser His Ser Phe Ser Phe Thr Phe Leu Glu Asp Leu Gln Ala Lys
 225 230 235 240
 Ile Leu Gly Ile Pro Tyr Lys Asn Asn Asp Leu Ser Met Phe Val Leu
 245 250 255
 Leu Pro Asn Asp Ile Asp Gly Leu Glu Lys Ile Ile Asp Lys Ile Ser
 260 265 270
 Pro Glu Lys Leu Val Glu Trp Thr Ser Pro Gly His Met Glu Glu Arg
 275 280 285
 Lys Val Asn Leu His Leu Pro Arg Phe Glu Val Glu Asp Ser Tyr Asp
 290 295 300
 Leu Glu Ala Val Leu Ala Ala Met Gly Met Gly Asp Ala Phe Ser Glu
 305 310 315 320
 His Lys Ala Asp Tyr Ser Gly Met Ser Ser Gly Ser Gly Leu Tyr Ala
 325 330 335
 Gln Lys Phe Leu His Ser Ser Phe Val Ala Val Thr Glu Glu Gly Thr
 340 345 350
 Glu Ala Ala Ala Thr Gly Ile Gly Phe Thr Val Thr Ser Ala Pro
 355 360 365
 Gly His Glu Asn Val His Cys Asn His Pro Phe Leu Phe Phe Ile Arg
 370 375 380
 His Asn Glu Ser Asn Ser Ile Leu Phe Phe Gly Arg Phe Ser Ser Pro
 385 390 395 400

<210> 113

<211> 957

<212> DNA

<213> Homo sapiens

<400> 113

ctgcaccttc tctgcacagc ggatgaaccc tgagcagctg aagaccagaa aagccactat 60
 gactttctgc ttaattcagg agcttacagg attcttcaaa gagtgtgtcc agcatccttt 120
 gaaacatgag ttcttaccag cagaagcaga cctttacccc accacctcag ctccaacagc 180
 agcaggtgaa acaaccagc cagcctccac ctccaggaat atttgttccc acaaccaggg 240
 agccatgccca ctcaagggtt ccacaacctg gaacacaaaa gattccagag ccaggctgtga 300
 caagggtccc tgagccaggc tgtaccaagg tccctgagcc aggttgtacc aaggtccctg 360
 agccaggatg taccagggtc cctgagccag gttgtaccaa ggctcctgag ccagggtaca 420
 caagggtccc tgagccaggc agcatcaagg tccctgacca aggtcttcac aagtttccctg 480
 agccagggtgc catcaaggtt cctgagcaag gatacaccaa agttcctgtg ccagggtaca 540
 caagggtacc agagccatgt ccttcaacgg tcactccagg cccagctcag cagaagacca 600
 agcagaagta atttgtgtga cagacaagcc cttgagaagc caaccaccag atgctggaca 660
 cctcttctcc atctgtttct gtgtcttaat tgtctgtaga ccttgtaatc atacattctt 720
 caccccaagg catagtctct ctcttatttg tatcctaaaa atacggtact ataaagcttt 780
 gtgtcacaca caactctgaag aatcctgtaa gccctgaat taagcagaaa gtcttcatgg 840
 cttttctggt ctctggctgc tcagggttca tctgaagatt cgaatgaaaa gaaatgcag 900
 tttcctgctc tgccctcatt aaattgcttt taattccaaa aaaaaaaaaa aaaaaaa 957

<210> 114
 <211> 161
 <212> PRT
 <213> Homo sapiens

<400> 114
 Met Ser Ser Tyr Gln Gln Lys Gln Thr Phe Thr Pro Pro Pro Gln Leu
 1 5 10 15
 Gln Gln Gln Gln Val Lys Gln Pro Ser Gln Pro Pro Pro Gln Glu Ile
 20 25 30
 Phe Val Pro Thr Thr Lys Glu Pro Cys His Ser Lys Val Pro Gln Pro
 35 40 45
 Gly Asn Thr Lys Ile Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 50 55 60
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 65 70 75 80
 Gly Cys Thr Lys Val Pro Glu Pro Gly Cys Thr Lys Val Pro Glu Pro
 85 90 95
 Gly Tyr Thr Lys Val Pro Glu Pro Gly Ser Ile Lys Val Pro Asp Gln
 100 105 110
 Gly Phe Ile Lys Phe Pro Glu Pro Gly Ala Ile Lys Val Pro Glu Gln
 115 120 125
 Gly Tyr Thr Lys Val Pro Val Pro Gly Tyr Thr Lys Val Pro Glu Pro
 130 135 140
 Cys Pro Ser Thr Val Thr Pro Gly Pro Ala Gln Lys Thr Lys Gln
 145 150 155 160
 Lys

<210> 115
 <211> 506
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 8, 21, 31, 32, 58, 75, 89, 96, 99, 103, 122, 126, 147, 150,
 158, 195, 210, 212, 219, 226, 246, 248, 249, 255, 258, 261,
 263, 265, 275, 304, 317, 321, 331, 337, 340, 358, 371, 377,
 380, 396, 450, 491
 <223> n = A,T,C or G

<400> 115
 cattggtnc ttcatttgct ntggaagtgt nnatctctaa cagtggacaa agttcccnct 60
 gccttaaac ctgtnacact ttgggaant gaaaantng tantatgata ggttattctg 120
 angtnaagat gtcttgata ccattanatt tgcgcccnct gtcagaggct catattgtgt 180
 tatgtaaatg gtatntcatt cgctactatn antcaatng aaatanggct ttggggttat 240
 gaatantng cagcncanct nanangctgt ctgtngtatt cattgtgtgc atagcacctc 300
 acancattgt aacctcnatc nagtgagaca nactagnaan ttctagtga tggctcanga 360
 ttccaaatgg notcatntcn aatgttttaa agttanttaa gtgtaagaaa tacagactgg 420
 atgttccacc aactagtacc tgtaatgacn ggctgtgcc aacacatctc ccttttccat 480
 gactgtgga ncccgcatcg gaaaaa 506

<210> 116
 <211> 3079
 <212> DNA

<213> Homo sapiens

<400> 116

```

ggatccccgg gtttctaaaa ccccccacag agtctctgcc aggccaaaga gcaaggaaaa 60
ggtcaaaagg cagaaaaaat gctgaggttag gaggagctat ggaaggataa acctggccct 120
aaagaggtca aagtgtgttta tagggggcgc tgaggagctat ccacatctctc tggcctaaac 180
cttgaggagca gctgctgccca gtgggctctgt ggaatagctgt gccttccctca acaaaaaaat 240
tgtgcacaaa aggtagaaac tctatctttcc ctctagcaca taaccaagaa tataaggtcta 300
cagatgtgcct ttccagagg gaaaacctgt gcgcaacctg ctgcctgcgaa aagtgtgaaga 360
cagatcaact ggggaatcgt ttgccccccg ctgtagggaca gcttccccaa gctccaagg 420
cagggtgctca catgtatccg tactgggatg gttgtcaata ctctgtgtcc ttgaagact 480
ccaggagcact gccatgccaa tgccccctca gttcctggca tctctttttg gctgcacaa 540
gccccagcct ctatggtgaa gacatacttg ctgacagcgt caccactttg ttgccaagg 600
atcagtgtct gaaggcaagg ttatttctaa ctgagcagag cctgccagga agaaagcgtt 660
tgacccccac accactgtgc aggtgtgacc ggtgagctca cagctgcccc ccaggcatgc 720
ccagcccaact taatcatcac agctcgacag ctctctcgcc cagcccagtt ctggaaggga 780
taaaaagggg catcaccggt cctgggttaac agagccacct tctgcgtcct gctgagctct 840
gttctctcca gcaacctcca accactagt gcttggttct ctgtctccac caggaacaag 900
ccaccatgtc tcgcagctca agtgtgtctt ccggagcggg gggcagtcgt agcttcagca 960
ccgctctcgc atgcacgcgt gcaccagctt caacctcggt tcccggtccg cctcctggag 1020
gggggtggcg tgggtgtgct ttggccaggg tcagccttgc ggggtcctgt gggatgggt 1080
gctatggcgc ccggagcctc tacaacctgg ggggtcctca gaggatctcc atcagcacta 1140
gtggtggcag cttcaggaa cggtttgggt ctggtgtctg agggcgctat ggctttggag 1200
gtggtggcgg tagtgattt ggtttcggcg gttggagctg ttgttgcttt gggctcgtgt 1260
gcggagctgt gcctggaggt ggcttcgggt gcctgtctgc ctctcgtgag cctcctggag 1320
gtatccaaga ggtcactgtc aaccagagtc tcttgactcc cctcaacctg caaatcgacc 1380
ccagatccca gagggtgagg accgagagac gcgagcagat caagaccctc aacaataagt 1440
ttgcctcctt catgcacaag gtgcggttcc tggagcagca gaacaaggtt ctggaacaaa 1500
agtggacocc gctgcaggag cagggccacca agactgtgag gcagaacctg gagccgttgt 1560
tcgaggcagta catcaacaac ctacgagggc agctggacag catcgtgggg gaacggggcc 1620
gcttgagactc agagctgaga aacatgcagg acctggttga agactcaag aacaagtatg 1680
aggatgaatc caacaaagctt accactgctg agaatgagtt tgtgatgctg aagaaggatg 1740
tagatgtctc ctacatgaac aaggtggagc tggaggccaa ggttgatgca ctgatggatg 1800
agattaactc catgaagatg ttctttgatg ccagatgcag acgatgtctc 1860
ctgacacctc agtggctctc tccatggaca acaaccgcaa cctggacctg gatagcatca 1920
tcgctgaggt caaggccacg tatgaggaga ttgccaaacc cagccggaca gaagccgagt 1980
cctggtatca gaccaagtat gaggagctgc agcagacagc tggccggcat ggcgatgacc 2040
tcgcacaacc caagcatgag atctctgaga tgaaccggat gatocaggag ctgagagccg 2100
agattgacaa tgtcaagaaa cagtgcgccca atctgcagaa cgccattcgg gatgccagc 2160
agcgtgggga ggtggccctc aaggatgcca ggaacaagct ggccgagctg gaggagcccg 2220
tgcaagaagg caagcaggac atggccccgc tgcgtcgtga gtaccaggag ctcatgaaca 2280
ccaagctggc cctggacgtg gagatcgcca ctaccgccaa gctgtcggag ggcgaggaa 2340
gcagactcgt tggagaagga gttggaccag gttgtgcaca tttgtgcaca acagatgtt 2400
cctctggata tggcagtggt agtggtctat gcggtggcct cggtggaggt ctggggggcg 2460
gctcgtgggt aggtcttgcc ggaggtagca tctctccagc ctactccagc agcagttagc 2520
gtgtcgccct aggtgtgtgg ctcatgttgg ggggtctcgg ctccagtgca agcagttagc 2580
gagggtctgg ggtggccttt ggcagtggtg ggggtagcag ctccagctgc aaatttgtct 2640
ccaccacctc ctctccccg aagagcttca agagctaaga acctgtgca agtcaactgc 2700
ttccaaagtc atccaaaccg ccatgggaga ttctccttc taggcagttg ctcaagccat 2760
gttttatcct tttctggaga gtactctaga ccaagccaat tgcaagaaca cattcttgg 2820
ttccaggag agcccaatc ccagccccgt gttcccgctg ccgcagttct atattctgt 2880
tcaaatcagc ctccaggtt ccacagcat ccacccaat ccaaaattt 2940
tcccaaatct aaatcatcaa aacagaatcc gtttttaaat atcaagttt 3000
taactacctc cagaatgtgt tctacccaa gttttttttt 3060

```

<210> 117

<211> 6921

<212> DNA

<213> Homo sapiens

<400> 117

gaattctgcac	tgtccactca	aaactttctat	tccgatcaaa	gctatctgtg	actacagaca	60
aatttgagata	accatttaca	aagacgatga	atgtgttttg	gcgaataact	ctcatcgtgc	120
taaatgggaag	gtcatttagtc	ctactgggaa	tgaggcgatg	gtcccatctg	ttgtgctcac	180
gcttctccca	ccaaacaaag	aagcgggtgga	ccttgccaac	agaatttgagc	aacagtataa	240
gaatgtccctg	acctttttggc	atgagtctca	cataaacatg	aagagtgtag	ttctcctggca	300
ttatctcatc	aatgaaattg	atagaattcg	agctagcaat	gtggctcaa	taagacaact	360
gctacctgtg	gaatcactgc	aagtttotaag	taatctacaa	tctcgttttg	aagattttct	420
ggaagatagc	caggaatccc	aagtcttttc	aggctcagat	ataacacaac	tggaaaagga	480
ggttaatgta	tgtaagcagt	attatcaaga	actctttaa	tctgcagaaa	gagagggaca	540
agaggaaatca	gtttataatc	tctacatctc	tgaagttcga	aacattagac	ttcggttaga	600
gaactgtgaa	gatcggctga	ttagacagat	togaactccc	ctggaaaagag	atgattttga	660
tgaaagtgtg	ttcagataca	cagaacagga	gaactaaag	aaagagctgg	aacgacttaa	720
agatgatttt	ggaacaatca	caaataaagt	tgaggagttt	ttcagtcag	cagcagcctc	780
ttcatcagtc	ccctccctac	gatcagagct	taatgtggtc	cttcagaaca	tgaaccaagt	840
ctattctatg	tcttccactt	acatagataa	gttgaaaact	gttaacttgg	tgtaaaaaaa	900
cactcaagct	gcagaagccc	tcgtaaaaact	ctatgaaact	aaactgtgtg	aagaagaagc	960
agttatagct	gacaagaata	atattgagaa	tctaataagt	actttaaagc	aatggagatc	1020
tgaagttagat	gaaaaagagc	aggtattcca	gcctttagag	gatgagttgc	agaaaagata	1080
agccatcagt	gatgaaatgt	ttaaaacgta	taaaagaacg	gaccttgatt	ttgactggca	1140
caaaagaaaa	gcagatcaat	tagttgaaag	gtggcaaaaa	gttcatgtgc	agattgacaa	1200
caggtttacgg	gaacttgagg	gcatttgcaa	tactcatgaag	tactcacagag	acacttacca	1260
tccttttagat	gattggatcc	agcaggttga	aactactcag	agaaagattc	aggaataatca	1320
gcctgaaaat	agtaaaaacc	tagccacaca	gttgatacca	cagaagatgc	tggtgtccga	1380
aatgaaatg	aaacagagca	aaatggacga	gtgtcaaaaa	tatgcagaac	agtcactcag	1440
tacagtgaag	gaactatgaat	tacaaacaat	gaacctacgg	gcgatgttag	attcacaaaca	1500
aaaactctcca	gtgaaacgccc	gaagaatgca	gagttcagca	gatctcatta	ttcaagagtt	1560
catggaacct	aggaactcgt	atctgcctc	ggtcaacttc	atgacacata	attataaatt	1620
tgctggtgat	tcatttgaaga	ggctgggaaga	ggaggagatt	aaaagtgta	aggagacctc	1680
tgaacatggg	gcataattcag	atctgcttca	gogtcagaag	gcaacagtcg	ttgagaatag	1740
caaaccttaca	ggaaagataa	gtgagttgga	aagaatggtg	gctgaaactaa	agaaacaaaa	1800
gtcccagata	gagggaagaac	ttccgaaggt	caggggaggct	gcagaaaatg	aattgagaaa	1860
gcagcagaga	aatgtgaaga	atatctctct	gcagaagata	agggtctgaaa	gtgaagccaa	1920
gcagtcacgc	agggaaacttg	aaaccattgt	gagagagaag	gaagcccgctg	aaagagaact	1980
ggaagcgggtg	agggcagctca	ccatagagggc	cgaggctaaa	agagctgcgcg	tggaaagaaa	2040
cctcctgaat	ttctgcgaatc	agtttgaggaa	aaacaccttt	accagacgaa	cacttggaaga	2100
tcactcttga	agaaaagaatt	taagtctcaa	tgattttgag	caacaaaaaa	ataaattaat	2160
ggaagaattta	agaaagaaga	gagacaatga	ggaagaactc	ttgaagctga	taaaagcagat	2220
ggaanaagac	cttgcatcttc	agaaacaggt	agcagagaaa	cagttgaaa	aaagcagaaa	2280
aattgaattg	gaagcagaaga	gaaaaataac	tgaaattcag	tatacatgta	gagaaaaatgc	2340
attgccaatg	ttgcgcatac	cacaggctac	atcatgcagg	gcagtaaacgg	gtctccagaca	2400
agaaactagc	agacagaaga	cagaagaact	caaacagcag	gtagatgaac	taacagctgc	2460
caatagaaag	gctgaacaa	acatgagaga	gctgacatat	gaacttaatg	ccctccagctg	2520
tgaaaaaacg	tcatctgagc	aaaaggctcg	tttgtcaaaa	gataaactag	attgacacaa	2580
taataacact	agatgtcctta	agtttgagct	ggaagaggag	gatcagcgcg	agaaagggta	2640
ttctcaacaa	ctcagagagc	ttggtaggca	attgaatcaa	accaacgcta	aagctgaaga	2700
agccatgcga	gaagcttagt	atctcaagaa	aataaagcgc	aattatcagt	tagaattaga	2760
atctcttaat	catgaaaaag	ggaaactaca	agagaagta	gacagaatca	caagggcaca	2820
tgctgtagct	gagaagaata	ttcagcattt	aaattccaaa	attcattctt	ttcgatgata	2880
gaagaattta	gaagagactac	aaatctgcga	gagaaaaatca	gatcatctaa	agaagacaatt	2940
tgaagaaagc	catgagcagt	tgcttcaaaa	tatcaaaagct	gaaaaagctt	ataatgataa	3000
aatccaaagg	ctcaatgaag	aatttgagaa	aagtaatgag	ttgtcagaga	tgctaaaaaca	3060
aaaagttagg	gagcttacta	ggcagataaa	tgaaacccaa	ttaatgtgag	agagaattca	3120
ggcagaatca	gagaatatag	ttttagagaa	acaaactatc	cagcaaaagt	gtgaagcaat	3180
gaaaattcag	gcagatgggt	ttaaagatca	gctacgcagc	acaaatgaac	acttgcataa	3240

acagacaaaa	acagagcagc	attttcaaa	aaaaattaaa	tgccatagaag	aagacctggc	3300
gaaagtgcaa	aatttggtaa	gtgaatttaa	gcaaaagtgt	gaccaacaga	acattatcat	3360
ccagaatacc	aagaaagaag	ttagaatctc	gaatgcggaa	ctgaatgcgt	ccaaagaaga	3420
gaagcgacgc	gggggacaga	aagttcagct	acaacaagct	caggttgcaag	agttaaataa	3480
caggttggaaa	aaagtacaag	acgaattaca	cttaaagacc	atagaggagc	agatgaccca	3540
ccagaagaat	gttctgttcc	aggaagaatc	tggttaattc	aaacaaatcg	cagaggaggt	3600
tcggaagaat	atggaaaaat	taatggagtc	caaatgcctc	actgaaaatg	atatttccag	3660
cattagagctt	gactttgtgt	ctcttcaaca	agaaaaactc	agagcccaag	aaaatgctaa	3720
gcttttggtaa	acaaaacata	agaactctga	aaagacagct	caacagatct	gtgaaacaa	3780
gcagcaaggg	gcacacatgg	aagcaaatca	ttacccaaaa	tgtoagaac	ttgaggatga	3840
cttagtagcc	agggacgctg	aggttgaaaa	ctgaaagcaa	aaaatggacc	acagatgcaa	3900
agagcatgaa	catcaattag	ttttgtccca	gtgtgaaatt	caaaaaaaga	gcacagccaa	3960
agactgtacc	ttcaaacag	attttgagat	gacagtgaag	gagtgccagc	actctggaga	4020
gctgtcctct	agaaaacact	gacacotcca	cccaacacc	agatccctcc	tggtgagatg	4080
gactcaagaa	ccacagccat	tggaaagaaa	gtggcagcat	cgggttggtg	aacagatacc	4140
caaaagaagt	caattccagc	caccaggggc	tcactcgag	aaagagaaaa	agacgagtg	4200
ttactctgag	tacttttctc	agacaagcac	cgagttacag	ataacttttg	atgagacaaa	4260
ccccattaca	agactgtctg	aaattgagaa	gataagagac	caagccctga	acaattctag	4320
accacctgtt	aggtatcaag	atacgcgatg	tgaattggaa	ctggtgaagg	ttttgacccc	4380
cttagagata	gctaaagaaca	agcagtatga	tatgcataca	gaagtcaaca	cattaaaaaa	4440
agaaaaaac	ccagttccca	gtctgaaga	atggatgctt	gaaggggtca	gagcatctgg	4500
tggtcatga	aaaggggatt	tccttaagaa	gggcttagaa	ccagagacct	tcagaaactt	4560
tgatggtgat	catcgatggt	cagtcaggga	tgatgaattt	aaattccaa	gctctaggca	4620
cactgtgact	gccagccgct	tggtggaaag	taagcttctg	gacatgagaa	caattggaga	4680
gctgcgactc	ggtcttaaga	ctgttgaaga	agtcagaaa	actcttaaca	agtttctgac	4740
gaaagccacc	tcaattgcag	ggctttacct	agaatctaca	aaagaaaaaa	tttcaattgc	4800
ctcagcggcc	gagagaaaca	taatagacaa	aatggtggct	ttggcatttt	tagaagctca	4860
ggctgcacaa	ggttttataa	ttgatcccat	ttcaggtcag	acatatctgt	ttgaagatgc	4920
ggttctttaa	ggagtgtgtg	accocgaatt	cagaatttagg	ctctcttggg	caggaagagc	4980
agctgtggga	tattcttatt	cttctaagac	attgtcagtg	tttcaagcta	tggaataatg	5040
aatgcttgac	agacaaaaag	gtaaacatat	cttggaaagc	cagatgtcca	gtgggggtgt	5100
cattgaccc	gtgagagcaa	ttctgtttcc	tcacagaatt	gctctgcagc	aggggtgtgt	5160
gaataatgcc	actctacagt	ttttacatga	gccatccagc	aaacacaag	ttttccctaa	5220
tcocaaataa	aagcaagctc	tgtattactc	agaattactg	cgaatgtgtg	tatttgatgt	5280
agagtcccaa	tgctttctgt	ttccatttgg	ggagaggaac	atttccaatc	tcaatgtcaa	5340
gaaaacacat	agaatttctg	tagtagatac	taaaacagga	tcagaattga	cogtgtagta	5400
ggctttccag	agaaacctga	ttgagaaaa	tatatatctt	gaactttcag	ggcagcaata	5460
tcagtggaag	gaagctatgt	tttttgaatc	ctatgggcat	ttcttccata	tgctgactga	5520
tactaaaaaa	ggatttacct	tcaattattaa	tgagggtata	gagcagggaa	caatttgcaa	5580
agcttggctc	aaaaagtatc	aggaagcctc	catcacactt	acagaaactc	ctgattcttt	5640
gctgagccgg	ttagtcccca	agaaagattt	gcacagtcct	gttgacagggt	attggctgac	5700
tgctatgggg	gaaagtagct	ctgtactaaa	agcctcccg	agaaatttgg	ttgatccgat	5760
tactgccctc	cgatgccctt	aagcccaagt	cagtaacagg	ggcataattg	atccctctac	5820
tgggcaaaa	taccgggttg	cogaagcttt	gcataagggc	ggcgttgatg	aggggtttgc	5880
ccagcagctg	cgacagtggt	aattagtaat	cacagggttg	ggccatccca	tcactaacaa	5940
aatgatgtca	gttggtggag	ctgtgaatgc	aaatattata	aatagggaaa	tggaatcccg	6000
atggttggaa	tttcagtact	tgacaggagg	gttgtagag	ccacaggttc	actctcggtt	6060
atcaatagaa	gaggtctctc	aagttaggtat	tatagatgtc	ctatgtgcca	aaaaactcaa	6120
agatacaaa	tcatatgtca	gaaataata	atgccctcag	acaaaaagaa	agttgacata	6180
taagaagacc	ttagaaaaag	ctgattttga	tttccacaca	ggactttaat	tgtagaagt	6240
atctgagccc	ctatgcacag	gaatttctag	ctctactact	ttctctacta	ggagcatggt	6300
taaataaact	tgcgaagggt	gatgcaggct	ggttcoatgc	actttttcag	agatgatgta	6360
tatcggtctac	atatgcactg	tgtgaattat	gtaacatact	ctatttctgt	aggcgtgcaa	6420
attgctaagt	gctcaaaaata	gagtaagttt	taaaattgaa	attacataag	atttaatgoc	6480
cttcaaatgg	tttcaatttag	ccttgagaat	ggttttttga	aacttggcca	cactaaaaatg	6540
tttttttttt	tttaactgata	atgtgggata	aacttgatga	actccaagtt	ccagatgtca	6600
tttcttcaga	actccccttc	attgaatagt	gatcatttat	taaatgataa	attgcatctg	6660
ctgaagaagc	acgtctgaaa	gcaccatgga	atccaaagaga	aagatataaa	ttcgttccca	6720

cagccttcaa	gctgcagtg	tttagattgc	ttcaaaaaat	gaaaaagttt	tgcccttttc	6780
gatatagtga	cctctctttgc	atattaaaa	gtttaccaca	atgtccatt	tctagttaag	6840
tcttcgcact	tgaaagctaa	cattatgaat	attatgtgtt	ggaggagggg	aaggatttcc	6900
ttcattctgt	gtattttccg	g				6921

<210> 118

<211> 946

<212> DNA

<213> Homo sapiens

<400> 118

cttctgactg	ggctcagggt	gacaggtaga	gctcaccatg	gcttcttctg	tcttctgtcc	60
ctccccatca	cagctgtggt	gcagtcacc	gtctccagtg	gctatggcgg	tgccagtggt	120
gtccgcagtg	gcttaggcct	gggtggagga	agcagctact	cctatggcag	tggtctttggc	180
gttgagggtg	gcttcagttc	cagcagtggt	agagccattg	ggggtggcct	cagctctgtt	240
ggaggcgga	gttcacocat	caagtacacc	accaactcct	cctccagcag	gaagagctat	300
aagcactaaa	gtgcgtctgc	tagctctcgg	tcaccacagtc	ctcaggcccc	tctctgtggt	360
cagagccctc	tctccaggtt	gctctgtctc	tctcggcctc	cagctctccc	tgctgtccca	420
ggtagagctg	gggatgaatg	cttagtgccc	tcactctctc	tctctctctc	taaccatct	480
gagcaccat	tgctccocat	cagatcaacc	tctgatttta	catcatgatg	taatcaacc	540
tgagacttca	ctgttactaa	attattaaat	tcttgctccc	agtgttctat	ctctgagggt	600
gagcattata	agaaaaatgac	ctctgctcct	tttcattgca	gaaaaatgcc	aggggcttat	660
ttcagaacaa	cttccactta	cttccactg	gctctcaaac	tctctaaatt	ataagtgttg	720
tgaaaccccca	cccagcgagt	atccatgaaa	gcacaagtga	ctagtccat	gatgtacaaa	780
gcctgtatct	ctgtgtgat	ttctgtgctc	ttcactgttt	gcaattgcta	ataaagcag	840
atttataata	catataattct	tttactttgc	cttgcttttg	ggccaaagtt	ttgggcttaa	900
acttttttat	ctgataagtg	aatagttggt	tttaaaagat	aatca		946

<210> 119

<211> 8948

<212> DNA

<213> Homo sapiens

<400> 119

tcacacagccc	ctgctccttg	ggccctccca	tgccatgcgc	taattctctcc	caccgcacca	60
acaccaacac	ccagctccga	cgagctcct	ctgcgcctt	gcgcctcc	gagccacagc	120
ttctctcccg	ctctcgccc	cgcccgctgc	cgtctccgc	gctcgcagcg	gcctcgaggag	180
ggcccgagta	gcgagcagcg	acctcgcgag	ccttcgcgac	tcgcccgccg	ttcccgccgc	240
gtccgcctat	ccttgccccc	ctccgctttc	tcggcgccgg	ccgcctcgc	ttatgcctcg	300
gcgctgagcg	gctccccga	ttgcccgccg	acatgagctg	caacggaggc	tcaccacccgc	360
ggatcaacac	ctctggcgcc	atgatccgcg	ccgagctctg	cccgacctgc	cgctacgagg	420
tgaccagcgt	cgccgggggc	accagcagga	tgatctatc	tcggcgccgc	gtgatccagc	480
accagaagct	ggacggctac	tgtaaaacgc	gcacgatg	caggcaccag	aaccagaaaca	540
ccatccagga	gctgctgcag	aactgctccg	actgcttgat	gcgagcagag	ctcatctgctg	600
agcctgaatt	gaagtatgga	gatggaaatc	aactgactcg	gagtcgagaa	ttggatgagt	660
gttttgcaca	ggccaatgac	caaatggaaa	tcctcgacag	cttgatcaga	gagatcgccg	720
agatggccca	gcccctgtgat	gcttaccaga	aaaggcttct	tcagctccaa	gagcaaatgc	780
gagcccttta	taaaagccat	agtgctccctc	gagtcgcgag	ggccagctcc	aagggtggtg	840
gaggtacac	ttgtccagagt	ggctctggct	gggatgagtt	caccaaacat	gtcaccagtg	900
aatgtttggg	gtggatgagg	cagcaaaagg	cggagatgga	catggtggcg	tggggtgtgg	960
acctgcccct	agtggagcag	cacattaaaca	gccaccgggg	catccacaac	tcacatcgccg	1020
actatcgctg	cgagctggac	aaaaatcaag	cgaactctgc	cgagaaatct	gcgatctacc	1080
agttggagga	ggagtatgaa	aaactgtcta	aagcgtcctt	tgagaggagt	gatcaactgc	1140
gacagctgca	gaacatcatt	caggccacgt	ccaggagagt	catgtggatc	aatgactctg	1200
aggagaggga	gctgctgtac	gactggagcg	acaagaacac	caacatcgct	cagaacacag	1260
aggcctctct	catacgcatg	agtcacactg	aagttaaaga	aaaagagctc	aataagctga	1320

aacaagaag	tgaccaact	gtctccaat	agcatccag	ttcagacaa	attgaggcct	1380
atatggacac	ttctgcagc	cagtgaggtt	ggattcttca	gatcaccaag	tgcatgtatg	1440
ttcatctgaa	agaaaatgt	gctcatcttc	agttttttga	agaggcgagc	tctcatgaag	1500
catacctgaa	gggctccag	gactccatca	ggaagaagta	ccctcgccac	agaacaatgc	1560
ccctgcagca	cctgctgaa	cagatcaagg	agctggagaa	agaacgagag	aaatccttg	1620
aatacaagcg	tcagggtcag	aacttggtaa	acaagctcaa	gaagatgtta	cagctgaagc	1680
ctctgtaaccc	agcaatacaga	agcaataaac	ccattattct	cagagctctc	tgtcgtaca	1740
aacaagatca	gaaaaatcgt	cataaggggg	atgagtgat	cctgaaggagc	aaacagagcg	1800
gcagcaagtg	gtactgtgac	ggccggggag	gcgttgacat	gcttgctccc	ctbtgtgggc	1860
tgatcatccc	tcctccgaac	ccactggccg	tggaacctct	ttcgaagatt	gagcagtact	1920
acgaagcact	cttggtcttc	tggaaccagc	ctacatcaa	catgaagagc	ctgtgtctct	1980
ggcactactg	catgattgac	atagagaaga	tcaggggccat	gacaatcgcc	aagctgaaaa	2040
caatgcggca	ggaagattac	atgaagacga	tagccgacct	tgagttacat	taccaagagt	2100
tcatacgaag	tgaccaaggc	tcagagatgt	ttggagatga	tgacaaggcg	aaaatacagt	2160
ctcagttcac	cgatgcccag	aagcattacc	agaccctggt	cattcagctc	ctgggtcttc	2220
cccgagccaa	gacagtgacc	acaactgaaa	tcactcatca	tggaacctgc	caagatgtca	2280
accataataa	agtaattgaa	accaacagag	aaaatgacaa	gcaagaacaa	tgagtgctga	2340
tgaggctgca	gaagattcgc	aggcagatag	agcactcgca	ggcgccggatg	actctcaaaa	2400
acotccctct	agcagaccag	gggtctcttc	accacatcac	agtgaataat	aacagatcta	2460
agagtgtgca	cttggtctca	caagcaattg	ctgaggttct	caaccagctt	aaagataatg	2520
ttgccaactc	caggagttct	gaaaagtaact	gctattttaca	gaatgaagta	tttgagctat	2580
ttcagaactc	ggaaaaatato	aatggtgttta	cagatggcta	cttaaatgca	ttatgcacag	2640
taaggggcact	gtccaggctc	attctccaaa	cagaagacat	gttaaaaggtt	tatgaagcca	2700
ggctcactga	ggaggaaaact	gtctgcctgg	acctggataa	agtggaaagct	taccgctgtg	2760
gactgaagaa	ataaaaaaat	gacttgaact	tgaagaagtc	gtgtgtggcc	actctgaaga	2820
cagaactaca	gaaagcccgag	cagatccaact	ctcagacttc	acagcagtat	ccaactttatg	2880
atctggactct	gggcaagttc	ggtgaaaaag	tcacacagct	gacagaccgc	tggaagagga	2940
tagataaaca	gatcgacttt	agattatggg	acctggagaa	acaaatcgaag	caattgagga	3000
attatctgta	ttaactctcag	gctttctcga	agtggtctcta	tgatcgttaa	gcgcgcagag	3060
atttccattaga	atccatgaaa	tttgagatt	ccaacacagt	catgcggttt	ttgaatgagc	3120
agaaagagct	gcacagtga	atatctggca	aacgagacaa	atcagaggaa	gtacaataaaa	3180
ttgtgaaact	ttgcgccaat	tcaattaagg	attatgagct	ccagctggcc	tcatacacct	3240
caggactggtc	aactctgtcg	aaacataccta	tcaaggagac	catgattcag	tccctctctg	3300
gggtgattat	gcaagaggct	gcagatgttc	atgctcggta	cattgaaact	cttacaagat	3360
ctggagacta	ttacaggttc	ttaagtgaag	tgctgaagag	tttggaagat	ctgaagctga	3420
aaaaatacaa	gatcgaagtt	ttggaagagg	agctcagact	ggcccggagt	gccaactcgg	3480
aaaaactgtaa	taagaacaaa	ttctctggatc	agaacctgca	gaaataccag	cgagagtgtt	3540
cccgatttcaa	agcgaaagctt	gcgagcctgg	aggagctgaa	gagacaggct	gacttgatg	3600
ggaagtgcgc	taagcaaaat	ctagacaaagt	gctacggcca	aataaaagaa	ctctaagga	3660
agatcacctcg	acctaactat	gagattgaag	atgaaaagag	agaagaagaaa	tctgtggag	3720
acagatttga	ccaacagaag	aatgactatg	accaactgca	gaaagcaagg	caatgtgaaa	3780
aggagaacact	tggttggcag	aaattagagt	ctgagaagag	catcaaggag	aaggagtacg	3840
agattgaaag	cttgagggtt	ctactgcag	aagaaggcac	ccggaagaga	gaatatgaaa	3900
atgagctggc	aaaggtaaga	aaccactata	atgaggagat	gagtaattta	aggaacaagt	3960
atgaacacaga	gatttaactt	acgaagacca	ccatcaagga	gatattccat	caaaaaggag	4020
atgatgtccaa	taattcttga	aaccagcttg	atagaacttc	aagggaataat	cgagattctga	4080
aggatgaagc	tgtcaggctc	aatgcagaca	ttctgcaggc	cactgagcag	caagggcgag	4140
ctgaagaaaa	cgcccttcag	caaaaaggct	gtggctctga	gataatgcag	agaagcagcg	4200
atctggagat	gaagactgaag	caggctcatgc	agcagcgctc	tgagagcaat	gcgcgcacaa	4260
agcagctccct	ggaggaggct	gccaaagacca	ttcaggacaa	aaataaggag	atcgagagac	4320
tcaaaagctga	gttttcaggag	gaggccaagc	ggcgtcgga	atatgaaaa	gaacttgatga	4380
aggtaagaaa	caattctgat	gaggagatca	ttagcttaaa	aaatcagttt	gagaccgaga	4440
tcacatcac	caagaccacc	atccaccagc	tcacatcgca	gaaggaaag	gatcacaggt	4500
ctccaccggc	tcagatagac	aatctcaccc	gagaaaaacag	gagcttatct	gaagaataaa	4560
agaggctgaa	gaacactcta	accagaccca	cgagaaatct	caggagggtg	gaagaagaca	4620
tcccaacgca	aaaggccact	ggctctgagg	tgtctcagag	gaacacagca	ctggaggttg	4680
agctgagaca	agtcactcag	atgcgaacag	aggagagcgt	aagatataag	caatctcttg	4740
atgatgctgc	caaaaccatc	caggataaaaa	acaaggagat	agaaaggtta	aaacaactga	4800

tcgacaaaga	aacaaatgac	cggaatgcc	tggaagatga	aaacgcgaga	ttacaaaggg	4860
tcacgatatga	cctgcagaaa	gcaaacagta	gtgcgacgga	gacaataaac	aaactgaagg	4920
ttcaggagca	agaactgaca	cgctgagga	tcgactatga	aagggtttcc	caggagagga	4980
ctgtgaagga	ccaggatatt	acgcggttcc	agaactctct	gaaagagctg	cagctgcaga	5040
agcagaaggt	ggaagaggag	ctgaatcgcc	tgaagaggac	cgctgcagaa	gaactcctga	5100
agaggagagga	gctggaggaa	gagctggaag	gcgatgaggag	gtcgctgaa	gagcaagcca	5160
tcaaaaatcac	caacctgacc	cagcagctgg	agcaggcatc	cattgttaag	aaaggagctg	5220
aggatgacct	ccggcagcag	agggcagctgc	tggatggcca	cctgagggaa	aagcagagga	5280
cccgaggaga	gctgaggagg	ctctcttctg	aggtcgaggc	cctgaggcgg	cagcttactcc	5340
aggaacacga	aagtgtcaaa	caagctcact	tagggaatga	gcatttcagc	aaggcgatcg	5400
aaagataaag	gaagccttta	aatgaagca	aaatagaaat	tgagagctgt	cagctctctca	5460
cagagaacct	gaccaaggag	cacttgatgt	tagaagaaga	actgcggaac	ctgagcgctgg	5520
agtacgatga	ctcgaggaga	ggacgaagcg	aagcggacag	tgataaaaat	goaacatct	5580
tggaactaag	gagocaggag	cagatcagca	acaacggagc	cttggaactg	caggggctga	5640
ttaatgtatt	acagagagag	agggaaaatt	tgagacagga	aattgagaaa	ttccaaaagc	5700
aggcttttag	gcgatctaatt	aggattcagg	aatcaaaaga	tcagtgactc	caggtgggtac	5760
aggaagaagga	gagccttctg	gtgaaaatca	aagtctctga	gcaagacaag	gcaaggctcg	5820
agaggctgga	ggatgcagctg	aatcgtgcga	aatcaactct	agaggcagcg	acagggtgta	5880
aaacgcyctc	ggagctgtag	aaacagcaaa	ttcagaatga	cctgaatcag	tgaagactcc	5940
aatattcccc	caaggaggag	gctattagga	agatagaatc	ggaagagaaa	aagagttaga	6000
gagagaagaa	cagctcttag	agtgcagctg	aaagactcca	agcagagatc	aaagaaatgt	6060
aaagagcgtg	caggcgtaag	ctggaggatt	ctaccaggga	gcacacgtca	cagtttagaaa	6120
cagaacgctc	ccgatattac	agggagattg	ataaactcag	acacgcgcca	tatgggtccc	6180
atcgagagac	ccagactgag	tgtgagtgga	ccgttgacac	ctccaagctg	gtgtttgtag	6240
ggctgaggaga	gaaggtgaca	gcaatgcagc	ttctatgagt	tcagctgact	gacaaaacaa	6300
ccctggacaa	actattgaag	gggaagaagt	cagtggaaga	agttgctctc	gaattccagc	6360
cattcctctg	gggtgcagga	ttctatcgctg	gagcatctgc	ttctctctaa	gaaaaatact	6420
ctttgttaga	ggccaagaga	aagaaattaa	tcagcccaga	atccacagct	atgctttctg	6480
agggccagcg	agctcacagt	ggtataattg	atcccaatcg	gaatgcagtc	ctgactgtcg	6540
acagtgccat	agctcggggc	ctcattgact	tcgatgacgc	tcagcagata	tatgcagcag	6600
aaaaagctat	cactggctttt	gatgatccat	tttcaggcaa	gcagtatctc	gtttcagaag	6660
ccatcaagaa	aaatttgatt	gatagagaaa	ccgggaatgc	cctgctggaa	gcccagattg	6720
cttcaggggg	tgtagttagc	cctgtgaaca	gtgtcttttt	gccaagagat	gtcgctctgg	6780
ccogggggct	gattgataga	gatttggatc	gatccctgaa	tgatccocga	gatagtgcga	6840
aaaaacttgt	ggatccagtc	accaaaaaga	aggttcagtt	cgtgcagctg	aaggaaacgt	6900
gcagaaatga	accataact	ggtctgctct	tgctttcagt	acagaagaga	agcatgtctc	6960
ttcaaggaaat	cagacaacct	gtgacgctca	ctgagctagt	agattctggt	atatgtagac	7020
cgctccactgt	caatgaaactg	gaatctggct	agattttctta	tgacgaggtg	ggtgagagaa	7080
ttaaaggactt	cctccagggt	tcaagctgca	tagcaggcat	atcaaatgag	accaccaaaa	7140
agaagctttg	catttatggt	gocattgaaa	ttgctttagt	cgacctctgt	actgctctgg	7200
agttgtctgga	agcccaagca	gctactggct	ttatagtgg	ttctgttagc	aacttgaggt	7260
taccagttgga	ggaagocctc	aaagaggctc	tggtgggcat	tgagttcaaa	gagaagcctc	7320
tgctctcaga	acgagctgtc	actgggtata	atgatcctga	acagggaac	atcatctctt	7380
tgttccaaag	catgaataag	gaaactcatc	aaaagggcca	cggatattcg	ttattagaag	7440
ccagagctga	aacccggggg	atcattgacc	caaaggagag	catcggttta	ccagtgacaa	7500
tagcatataa	gaggggctat	ttcaatgagg	actcagtgga	tattctctca	gatccaagtg	7560
atgatatacaa	agattttttt	gaccccaaca	ctgaagaaaa	ttttacactat	ctgcacaacta	7620
gaagaagaat	catttaaggat	gaggaacaag	ggctctgtct	ctgtcctctg	aaagaaaaga	7680
agaaacaggt	gcagacatca	caaaagaata	ccctcaggaa	gcgtagagtg	gtcatagttg	7740
accocagaac	caataaagaa	atgtctgttc	aggaggccta	caagaagggc	ctaattgatt	7800
atgaaacctt	caaaagactg	tgtgagcagg	aatgtgaatg	ggaagaaata	accatcacgg	7860
gatcacagct	ctccacagtg	gtggctcctg	tagatagaaa	gcaggcgagt	cagttatgata	7920
ttcaagatgt	tattgacaag	ggcctttgtt	acagggaatt	ctttgatcag	taccgctgg	7980
gcagcctcag	cctccatcaa	tttgctgaca	tgatctcctt	gaaaaatgt	ctgcggacca	8040
gcagcagcat	gggcagttgt	gtcagcgatg	atgtttttac	cagctccocga	catgaatcag	8100
taagttaagat	ttccaccata	tcacgagctca	ggaatttaac	cataaggcag	agctctttttt	8160
cagacacccct	ggaagaatcg	agccccattg	cagccattct	tgacacagaa	aaactgagga	8220
aaatctccat	tacagaaggt	atagagcggg	gcactgttga	cagcatcacg	ggtcagaggc	8280

```

ttctggaggc tcaggcctgc acaggtggca tcatccacc aaccacgggc cagaagctgt 8340
cacttcagga cgcagctctcc caggggtgtga ttgaccaaga catggccaacc agcgtgaagc 8400
ctgctcagaa agccttcata ggcttcgagg gtgtgaagg aaagaagaag atgtcagcag 8460
cagagggcagt gaaagaaaaa tggctcccg atgaggctgg ccagcgcttc ctggagttcc 8520
agtacctcac gggaggtctt gttagcccg aagtgcctgg gaggataagc accgaagaag 8580
ccatccggaa ggggttcata gatggcccg cgcacagag gctcgaagc accagcagct 8640
atgccaaaat cctgacctgc cccaaaacca aattaaaaat atcctataag gatgccataa 8700
atcgctccat ggtagaagat atcactgggc tgcgcctctt ggaagccgcc tccgtgtcgt 8760
ccaagggctt acccagccct taccaaatgt cttaggctcc ggggtccgc ctgggctccc 8820
gctcggcgta tgcctccgga tctcgtccg ggtcccgag tgggtcccg agaggaagct 8880
ttgaccgcac agggaaattct tctactctt attcctaact atttagcagt agttctatgt 8940
ggcaactag

```

```

<210> 120
<211> 587
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 91, 131, 256, 263, 332, 392, 400, 403, 461, 496, 497, 499,
510, 511, 518, 519, 539, 554, 560, 576
<223> n = A,T,C or G

```

```

<400> 120
cgtctcaagc acttagacta catcaggga gaacacagac cacatccctg tctcatgctg 60
gcttatgttt tctggaagaa agtggagacc nagtctgttg ctttagggct cccgggctg 120
gggctgtgca ntccggtcag ggcgggaagg gaaatgcacc gctgcatgtg aactacagc 180
ccaggcgagt gcccttccc ttagcactac ctggcctcct gcctccctc gctcatgttt 240
cctccaccct tcaanaaatg aanaaccoca tgggcccgag ccttggccct ggggaaccaa 300
ggcagccttc caaaactcag gggctgaagc anaactattg ggcaggggct gactttgggt 360
gacactgccc attccctctc agggcagctc angtoaccn ggnctcttga acccagcctg 420
ttcctttgaa aaagggcaaa actgaaaagg gcttttccca naaaaagaaa aaccagggaa 480
ctttggcgag gcttcnntnt taccaaaacn ncttctcnng gatttttaag tcccattng 540
gctccactt accngggcn atgccccaaa attaanaatt tcccatc 587

```

```

<210> 121
<211> 619
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 260, 527, 560, 564, 566, 585, 599
<223> n = A,T,C or G

```

```

<400> 121
cactagttag atagaacac tgtgtccga gagtaaggag agaagctact attgattaga 60
gcctaaccac ggttaactgc aagaagaggc gggatacttt cagctttoca tgtaactgta 120
tgcataaagc caatgtagtc cagtttctaa gatcatgttc caagctcaact gaatcccaact 180
tcaatcacac ctcatgaact cctgatggaa caataacagc cccaagcctg tggtatgatg 240
tgcaactctg ctgactctcan aaaaaatct actctcataa atgggtggga gtattttggg 300
gacaacctac ttgtcttggc tgagtgaagg aatgatattc atatattcat ttattccatg 360
gacatttagt tagtgctttt tatataccag gcatgatgct gagtgcactc cttgtgtata 420
tttccaaatt tttgtacagt cgtcgacat atttgaatc atatattaa acttccaaaa 480
aatgaagtcc ctgggttttc atggcaactt gatcagtaaa ggattcnctc ctgttttgta 540

```

cttaaaacat ctactatatn gttanatga aattcctttt cccnccctcc cgaaaaaana 600
aagtgtgtgg gaaaaaaa 619

<210> 122

<211> 1475

<212> DNA

<213> Homo sapiens

<400> 122

tccacctgtc cccgcagcgc cgtctcgcgc cctcctgcgc cagccaccca gccgccgtct 60
agcccccga cctgcgcacc atgagagccc tgtgtgcgcg cctgcttctc tgcgtctctg 120
tcgtgagcga ctccaaagcg agcaatgaac ttcatcaagt tccatcgaaac tgtgaactgtc 180
taaatggagc aacatgtgtg tccaacaagt acttctccaa cattcactgg tgcgaactgcc 240
caaaagaatt cggagggcag cactgtgaaa tagataagtc aaaaacctgc tatgagggga 300
atggtcactt ttacogagga aaggccagca ctgacaccaa gggccggccc tgcctgccc 360
ggaaactctc cactgtcctt cagcaaacgt accatgcccc cagatctgat gctcttcagc 420
tggtgctggg gaaacataat tactcgagga acccagacaa ccggaggcga cctgtgtgct 480
atgtgcaggt gggcctaaaag ccgcttctcc aagagtgcac ggtgcagtac tgcgcagatg 540
gaaaaagccc ctctctctct ccagaagaat taaaatttca gtgtggccaa aagactctga 600
ggccccgctt taagattatt gggggagaat tcaccaccaa cgagaaccag cctgtgtttg 660
cgcccatcta caggaggcac cgggggggct ctgtcaccta cgtgtgtgga ggcagcctca 720
tcagcccttg ctgggtgatc agccccaac actgcttcat tgattaccca aagaaggagg 780
actacatcgt ctacctgggt cgtcaaggc ttaactccaa cagcaaggg gagatgaagt 840
ttgaggttga aaacctcacc ctacacaagg actacagcgc tgacacgctt gctcaccaga 900
acgacattgc cttgtcgagg atccgttcca aggagggcag gttgctgcag cctcccgcga 960
ctatcacagc catctgcctg cctcgtatgt ataacgatcc ccagtttggc acaagctgtg 1020
cgactcaggt ctttggaaaa gagaattcta cgcactatct ctatccgagat tgcgcaga 1080
tgactgttgt gaagctgatt tccccccgg agtgtcagca gccccactac taoggtctgt 1140
aagtcaccac caaaatgctg tgtgctgctg acccagcagt gaaaaacagt tctgtccagg 1200
gagactcagg gggaccocct gtctgttccc tccaaggcgc catgactttg actggaattg 1260
tgactgtggc ccgtggatgc gccctgaagg cccctacagg aggtctacag agagtctaac 1320
acttcttacc ctggactccc agtcacacca aggaagagaa tggcctggcc ctctgagggt 1380
ccccagggag gaaacgggca ccaccgcctt tctgtctgtg tgtcattttt gcagtagagt 1440
catctccatc agctgtaaga agagactggg aagat 1475

<210> 123

<211> 2294

<212> DNA

<213> Homo sapiens

<400> 123

cagcgcgcgc tcgcgccctc ctgcgcgcgc caccagcgcg ccgtctagcg ccccgacctc 60
gccaccatga gagccctgct ggccgcgcctg ctctctctgc tctgtgtcgt gagcgactcc 120
aaaggctcga atgaacttca tcaagtcca tcgaactgtg actgtctaaa tggaggaaaca 180
tgtgtgtcca acaagtactt ctccaaacct cactggtgca cctgcccaga gaaattcgga 240
gggcagcact gtgaaataga taagtcaaaa acctgctatg aggggaattg tcaactttac 300
cgaggaaagg ccagcactga caccatgggc cgcctctgcc cggcctggaa ctctgccact 360
gtccttcagc aaacgtacca tgccacaga tctgatgtct ttcatgtgg cctggggaaa 420
cataattact gcaggaaacc agacaacccg aggcgacctg ggtgctatgt cagagtgggc 480
ctaaagccgc ttgtccaaga gtgcattggt catgactgcg cagatggaaa aaagccctcc 540
tctcctccag aagaattaaa atttcagtgt ggccaaaaga cctctgaggg ccgctttaa 600
attatgtggg gagaattcac caccatcgag aaccagccct gctttgcgcg catctacagg 660
agggcaccgg ggggctctgt caccatcgtg tgtggaggca gctcatcag ccttctgtg 720
gtgatcagc ccacacactg ctctcattgat tacccaaga aggaggacta catgctctac 780
ctgggtcgct caaggcttaa ctccaacacg caaggggaga tgaagtttga ggtggaaaa 840
ctaactctac acaaggacta cagcgtgac acgcttgctc accacaaga catgtcctg 900
ctgaagatcc gttccaagga gggcaggtgt gcgcagccat cccgagctat acagaccatc 960
tgctgtccct cgatgtataa cgatcccccag tttggacaaa gctgtgagat cactggcctt 1020

```

ggaaaaagaga atttaccga ctatctctat ccggagcagc tgaatatgac tgttgtaag 1080
ctgatttccc accgggagtg tcagcagccc cactactacg gctctgaagt ccaccacaaa 1140
atgctgtgtg ctgctgacc acagtggaaa acagatttct gccaggggaga ctcaggggga 1200
ccctctgtct gtctctcca aggcgcgatg actttgactg gaattgtgag ctggggccgt 1260
ggatgtgccc tgaaggacaa gccaggcgctc tacacgagag tctcacactt cttacccttg 1320
atccgcagtc acaccagga agagaatggc ctggccctct gaggggtccc agggaggaaa 1380
cgggaccacc cogctttctt gctggttgct attttgcagt agagtcatct ccatcagctg 1440
taagaagagc tgggaatata ggctctgcac agatggattt gcctgtgcca ccaccaggcg 1500
gaacgacaat agctttacc tcaggcatag gctgggtgc tggctgcccc gaccctcttg 1560
gccaggatgg aggggtggct cgtactcaac atgttactga ccagcaactt gcttttttct 1620
ggactgaagc ctgcaggagt taaaaaggcg agggcatctc ctgtgcatgg gctcgaaggg 1680
agagccagct ccccccagcg gtgggcattt gtgaggccca tggttgagaa atgaataatt 1740
tcccaattag gaagtgttaag cagctgaggt ctcttgagg agcttgacca atgtggagcg 1800
agcggtttgg ggagcagaga cactaacgac ttcaggcgag ggctctgata ttcatgaat 1860
gtatcaggaa atatatatgt gtgtgtatgt ttgcacactt gtgtgtgggc tgtgagtgt 1920
agtgtagta agagctgggt tctgattggt aagtctaaat attccttaa actgtgtgga 1980
ctgtgatgcc acacagagtg gtctttcttg agagggtata ggtaactcct ggggcctctt 2040
gggtccccc agtgacagtg cctgggaatg tattattctg cagcaatgac ttgtgaccag 2100
actgtctcag ttctacttct acatagatgt cctttctctg gccagttatc ccttctcttt 2160
agcctagttc atccaatcct cactgggtgg gtgaggacc actcctgtac actgaatatt 2220
tatattttcc tatttttatt tatatttttg taatttttaa taaagtgtat caataaaatg 2280
tgatttttct gatg 2294

```

<210> 124

<211> 956

<212> DNA

<213> Homo sapiens

<400> 124

```

gatgagttcc gcaccaagtt tgagacagac caggccctgc gctgagtggt ggaggccgac 60
atcaatggcc tgcgcagggt gctggatgag ctgaccctgg ccagagccga cctggagatg 120
cagatttgaga acctcaagga ggagctggcc tacctgaaga agaaccoca ggaggagatg 180
aacgccctgc gaggccaggt ggggtggtgag atcaatgtgg agatggagc tgccccagcg 240
gtggacctga gcgcgcatct caacgagatg cgtgaccagt atgagaagt ggagagaaag 300
aacgccgaag atgccgagga ttggttcttc agcaagacag aggaactgaa ccgcgaggtg 360
gccaccaaca gtgagctggt gcagagtggc aagagtgaga tctcgagct ccgcgccacc 420
atgcaggcct tggagataga gctgcagtc cagctcagca tgaagatc cctggaggcg 480
aacctggcgg agacagagaa ccgctaactg gtgcagctgt ccagatcca ggggctgatt 540
ggcagcgttg aggagcagct ggcacagctt cgtctgcaga tggagcagca gaaccaggaa 600
tacaaaatcc tgctggatgt gaagacgcgg ctggagcagg agattgccac ctaccgcgcg 660
ctgtcggagg gagaggtatg ccacctgact cagtacaaga aagaacccgt gaccaccctg 720
caggtgcgta ccatctgga agaggtccag gatggcaagg tcatctctc ccgcgagcag 780
gtccacaga ccaccgcgtg aggactcaag taccocggcc gccaccaccg gaggcaggga 840
cgagcgcgcg ccatctgcc ccagctctcc ggctctcca gctcagccc cctgctctcg 900
tcccttcccc atgcttctt gctgatgac aataaaagct tgttgactca ctatg 956

```

<210> 125

<211> 486

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 16

<223> n = A,T,C or G

<400> 125

```

aaattatata tagtgnttca gctcccattg ttggtgttcat agtcttctag gaacagataa 60

```

acttaagtat	tcaattoact	cttggcattt	tttctttaat	ataggctttt	tagcctattt	120
ttgaaaaact	gcttttcttc	tgagacacct	attctgaatg	tcatacaact	taccaaaact	180
tctaagtcca	gagctaactt	agtactgttt	aagttaactt	tgactgaatt	ttcttctatt	240
tctgttttagc	cagtggttacc	aaggttaagct	ggggaatgaa	gtataccaac	ttctttcaga	300
gcatttttagg	acatttatggc	agcttttagaa	ggctgtcttg	tttctagcca	agggagagcc	360
agcgcaggtt	ttggatacta	gagaaagtca	tttgcttgta	ctattgccat	tttagaagac	420
tctgatgtga	attcaaatatt	tacctctgtt	acttaaaagcc	aacaatttta	aggcagtagt	480
tttact						486

<210> 126

<211> 3552

<212> DNA

<213> Homo sapiens

<400> 126

cggcaggcag	gtctcgtctc	ggcaccctcc	cgccgcccgc	gttctctctg	cctgcgcccg	60
catcccgatg	gcgcgcgctg	ggcccccggg	ctccgtgcgc	ggagccgctc	gcctgcattc	120
gotcgtgacc	ctcgtgatct	tcagtgctgc	tggtgaagcc	tgcaaaaagg	tgatacttaa	180
tgtaacctct	aaactagagg	cagacaaaat	aattggcaga	gttaatttgg	aagagtgcct	240
cagggtctgca	gacctcatcc	ggccaagtga	tctcgtattc	agagtttcca	atgatgggtc	300
agtgtaacaca	gccaggcgct	ttgcgcgtgc	tgataagaaa	agatcattta	ccatattggc	360
ttctgacaaa	aggaacacaga	cacagaaaga	ggttactctg	ctgctagaaac	atcagaagaa	420
ggatatcgaa	acaagacaca	ctagagaaac	tgttctcagg	cgtgccaaaga	ggagatgggc	480
acctattctc	tgctctatgc	aagagaattc	cttggggcct	ttcccatctg	ttctctcaaca	540
agttgaattct	gatgcagcac	agaactatcc	tgctctctac	tcataaagtg	gcagctggagt	600
tgataaagaa	ccctttaaatt	tgttttatat	agaaagagac	actggaatac	tattttgcac	660
tcggcctctg	gatcgtgaag	aatatgatgt	ttttgatctt	attgcttatg	cgctcaactgc	720
agatggatat	tcagcagatc	tgccctctcc	actaccctac	agggttagag	atgaaaatga	780
caaccacacct	gttttcacag	aagcaattta	taattttgaa	gttttggaaa	ctagtagacc	840
tggtactaca	gtgggggtgg	tttgtgccac	agacagagat	gaaccggaca	caatgcatac	900
gcgcctgaaa	tacagcattt	tgacgcagac	accaaagttca	cctgggctct	tttctgtgca	960
tcocagacaca	ggcgtaatca	ccacagctct	tcattatttg	gacagagagg	ttgtagacaa	1020
gtactcattg	ataatgaag	tacaagacat	ggatggccag	ttttttggat	tgataggacc	1080
atcaacttgt	atcataacag	taacagattc	aaatgataat	gcaccacctt	tcagacaaaa	1140
tgcttatgaa	gcatttgtag	agggaaaatgc	attcaattgt	gaaatcttcc	gaatacctat	1200
agaagataag	gatttaatta	acactgcccac	ttggagagtc	aatttttaca	ttttaaagg	1260
aaatgaaaaat	ggacatttca	aaatcagcac	agacaaaaga	actaatgaag	gtgtctcttc	1320
tggttgaaag	ccaactgaatt	atgaagaaaa	ccgtcaagtg	aacctggaaa	ttggagttaa	1380
caatgaagcg	ccattttgcta	gagatattcc	cagagtgaac	gccttgaaca	gagccttggt	1440
tcacgttcat	gtgagggatc	tggaatgggg	gcctgaatgc	actcctcgac	cccaatagct	1500
gcggattaaa	gaaaacttag	cagtggggtc	aaagatcaac	ggctataaag	caatgacccc	1560
cgaaaaataga	aatggcgaat	gtttaaggta	caaaaatttg	catgatccca	aaggttggat	1620
caacatttgt	gaaatttcaag	ggccaatcat	aatctccaaa	atcctggata	gggaggttga	1680
aaactccaaa	aatagtttgt	ataattatc	agtcctggca	atagacaaaag	atgatagatc	1740
attgactctga	acaactctctg	tgaacattga	agatgtaaat	gataatccac	gagaataact	1800
tcagaataat	gtatgcattt	gcaaaacaaa	aatggggtat	accgacattt	tagctgttga	1860
tcctgatgaa	ctgttccatt	gagctccatt	ttatttcagt	ttgcaccaata	cttctccaga	1920
aatcaagtga	ctgtggagcc	tcacaaaagt	taatgatata	gctgcccgct	tttcataatc	1980
gaaaatgct	ggattttcaag	aatataccat	tcctattact	gtaaaagaca	gggcccggca	2040
agctgcacaa	aaattattga	gagttaatct	gtgtgaattg	actcaatccaa	ctcagtgtcg	2100
tggaacttca	aggagatagc	gagtaatact	tggaataatg	gcaatctact	caatatctact	2160
gggtatagca	ctgctctttt	ctgtattgct	aaactttaga	tgtggagctt	ttgtgtcaac	2220
taaaagggaaa	cytttttctg	aagatttagc	acagcaaaaac	ttaattatata	caaacacaga	2280
agcaactgga	gcagcatagag	tgctgtctgc	caatggattt	atgacccaaa	ctaccacaaa	2340
ctctagccaaa	ggttttttgt	gtactatggg	atcagggaatg	aaaaatggag	ggcagggaac	2400
cattgaaatg	atgaaaggag	gaaaccagac	cttggaatcc	tgccgggggg	ctgggcatca	2460
tcataccctg	gactcctgca	ggggaggaca	cacggagggtg	gacaactgca	gatacaacta	2520
ctcggagtg	cacagtttta	ctcaaccccg	tctcgttgaa	aaattgcact	gatgtaatac	2580

```

gaatgaagac cgcgatccat cccaagatta tgtcctcact tataactatg aggggaagagg 2640
atctccagct ggcttcgtgg gctgctgcag tgaaaagcag gaagaagatg gocttgactt 2700
tttaaaataat ttggaaccca aatttattac attagcagaa gcattgcacaa agagataaatg 2760
tcacagtgtc acaattaggt ctttgtcaga caattctggag gttccaaaaa ataataattgt 2820
aaagtccaat ttcaacatgt atgtatatga tgattttttt tccaattttg aattatgcta 2880
ctcaccatatt tatattttta aagcaagttg ttgcttatct ttccaaaaaa gtgaaaaatg 2940
ttaaaaacaga caactggtaa atctcaaaact ccagcactgg aattaaggtc tctaaagcat 3000
ctgtctcttt ttttttttac agatattttta gtaataaata tgctgggataa atattagctc 3060
aacaatagct aagttatgct aatatoacat tattatgtat tcacttttaag tgatagttaa 3120
aaaaataaac aagaatatatt gagtatoact atgtgaagaa agttttggaa aagaacaact 3180
gaagactgaa ttaaaattaaa aatgttgtag ctcataaaga attggactca cccctactgc 3240
actaccaaat tcaatttgact ttggaggcaa aatgtgttga agtgcctcat gaagtagcaa 3300
ttttctatag gaatatagtt ggaataaact gtgtgtgtgt atattattat taactaatgc 3360
aatattttaaa tgaatgaga acaaagagga aaatggtaaa aacttgaat gaggctgggg 3420
tatagtttgt cctacaatag aaaaaagaga gagcttctca ggctggggct cttaaatgct 3480
gcattataac tgagtctatg aggaatatgt tctgtgccaa ttgtgttaat ttgtttaaaa 3540
tgttaataaa at 3552

```

<210> 127

<211> 754

<212> DNA

<213> Homo sapiens

<400> 127

```

tttttttttt ttgtcattgt tcattgattt taatgagaaa gctaagagag gaaataagta 60
gcccttccaaa gggtcacacag aagtaagtga cagatccagg attcataatc aagcattctg 120
gctctagtgt ccatgtctct caaccattat gacccaatat tcaaccaaact caatactgaa 180
ggacacgtga aatgtatccg gtattttact attacaacaa aaaatccaat gaacattctt 240
gaagacatac acaaaaaataa tggttacaat agaagttact ggaattgaaa tttttgtcca 300
acctatatta aaatgtaaag cttttgatat agctaataga tttttgaaat gatcagttct 360
aacgttttga ggggagcaca ctctgcactg gggaaaagat tcaactgtgaa gcaagagca 420
cctttatggt tggatcatct tgtcattaaa gtccaggcgt tatctatctt gtaagtggca 480
gaatcaagac tgcaatatcg cctgcttttc tttttaactc atgttttccc ttgactacac 540
tggtctccaa agtaaaaccc ctgtgtcagt gtaactattca tggaatactc tgcaattata 600
acacacttct aatactttta atacccaatc aaaatttatt atacatatgt atcatagata 660
ctcatctgta aagctgtgct tcaaaatagt gatctcttcc caacattaca atatatatta 720
atgatgtcga acctgcctgc ggcgcgcctc gaag 754

```

<210> 128

<211> 374

<212> DNA

<213> Homo sapiens

<400> 128

```

aggttttgat taaaaaggca aatgatttta ttgttcgata atcttttaaa aaaataagag 60
gaaggagtaa aattaaagat gaaagatgat ttttatttcc ttgtgacctc tatatcccc 120
ttcccttgcc cttggtaagt aactcttgat ggagaaagga ttaaaagactc ttatttaacc 180
aaaaaacaga gccagtaaat catttccaaa gggttagtato tccctgtcta cctcttcttt 240
ggttttaattg aataaaacta tatgttcata tatgtattaa acaactcag aataacatct 300
tttctctctt agttaaggca ttataagggc tatactatca tccataataa ccaaggcaat 360
aacttaaaaa gctg 374

```

<210> 129

<211> 546

<212> DNA

<213> Homo sapiens

<400> 129

agtgtgatgt	atatctgcag	aattcgggct	aagcgtggct	gcgcccgag	gtctggaact	60
tccagcac	tgaaggag	cctcctgagc	tgactcggct	aaagccccac	tttcgctcct	120
ctctatttct	gctactgat	ttccttggag	cattcatctg	aatattaccg	tttgcgtgtg	180
aaacctggtac	atacatagca	tgactccctg	gaatagagtg	ggctgggggt	cttatgctgg	240
gagagtgtatt	gacatgcact	ttcaagctat	atctaccatt	tgacgcaaa	gagaaaaaat	300
acctcgagta	aattccatca	ttttttataa	catcagcacc	tgctccatca	tcaaggagtc	360
tcagcgttaac	aggatctcca	gtctctggct	caactctggc	agtgacagtg	goacttaagaa	420
tgggataaaa	ttccctgttc	acattggcat	aaatcatcac	aggatgagga	aaatggaggc	480
tgctctcttc	cacaaaggct	ttccacagtg	ctggggggcac	agacctgcc	ggggcgccgc	540
tcgaaa						546

<210> 130

<211> 5156

<212> DNA

<213> Homo sapiens

<400> 130

accaaaccgag	gcgccgggca	gcgacccctg	cagcgagagc	agagactgag	cggcccgcca	60
ccgcgatgcc	tgcgctctgt	ctgggctgct	gcctctgctt	gtcgctctctc	ctgcccgcag	120
cccggggccac	ctccaggagg	gaagtctgtg	attgcaatgg	gaagtcacag	gactgtatct	180
ttgatcgggga	acttccacga	caaatctggt	atggattccg	ctgcctcaac	tgcaatgaca	240
acactgagtgc	cattcactgc	gagaagtgtca	agaatggctt	ttaccggcac	agagaagaagg	300
accgctgttt	gccctgcaat	tgtaactcca	aaggttctct	tagtgctcga	tgtgacaaat	360
ccggacgggt	cagctgtaaa	ccagggtgtga	caggagccag	atgcgaccca	tgctgtgccag	420
gcttccacat	ctccagggat	gcggggtgtca	cccaagacca	gagactgtca	gactccaagt	480
gtgactgtga	ccacagctgc	atccgagggc	cctgtgacgc	ggggcgctgt	gtctgcaagc	540
cagctgtccac	tggaagaacg	tgtgataggt	ctcgatcagg	ttactataat	ctggatgggg	600
ggaacccctga	gggctgtacc	cagtgtttct	gctatgggca	ttcagccagc	tgccgcagct	660
ctcgagaata	caggttccat	aagatcaact	ctacctttca	tcagatgttt	gatgtctgga	720
aggctgtcca	acgaaatggg	tctcctgcaa	agctccaatg	gtcacagcgc	catcaagatg	780
tgtttagctc	agcccaacga	ctagaccctg	tctattttgt	ggctcccgac	aaatttctct	840
ggaatcaaca	ggtgagctat	ggtcaaaagc	tgtctcttga	ctaccgtgtg	gacagaggag	900
gcagacaccc	atctgcccat	gatgtgatcc	tggaaggtgc	tggtctacgg	atcacagctc	960
octtgatgcc	acttggcaag	acactgcott	gtgggctcac	caagacttac	acattcaggt	1020
taaatgagca	tccaagcaat	aattggaagc	ccagctgag	ttacttttag	tatcgaaggt	1080
tactcgggaa	tctcacagcc	ctccgcatac	gagctacata	tggaagaatc	agtgactgtt	1140
acattgacaa	tgtgacctgt	atttcagccc	gcctctgtct	tggaagccca	gcacctgggg	1200
ttgaacagtg	tatatgtctc	gttgggtaca	aggggcaatt	ctgccaggtg	tgtgtctctg	1260
gtcacaaag	agattcagcg	agactggggc	cttttggcac	ctgtattctc	tgtaactctc	1320
aagggggagg	ggctctgatg	ccagacacag	gagattgtta	ttcaggccag	gagaactcgt	1380
acattgagtg	tgctgactgc	ccaattggtt	tctacaaaga	tcgcagcgac	cccgcgagct	1440
gcaagccatg	ttccctgtat	aaagggttca	gctgctcagt	gatgcgggag	acgggaggag	1500
tggtgtgcga	taactgcctc	ccgggggtca	ccggtgcgcc	ctgtgagctg	tgctgtgatg	1560
gtactcttgg	ggagcccttt	ggtgaacatg	gccagtgtag	gccttgtagc	ccctgtcaat	1620
gcaacaacaa	tgtgagcccc	agtgctctgt	ggaaattgtga	ccgctcgaca	ggcaggtgtt	1680
tgaagtgtat	ccacaacaca	gcgggcattc	actgogacca	gtgcaaaaga	ggctactctg	1740
gggagcccat	ggctcccaac	ccagcacaga	agtgctgcag	ttgcaactgt	aaccccaagg	1800
gtccagagcg	tgtaggatgt	cgaagtgtat	gcacctgtgt	ttgcaagcca	ggattttggg	1860
gcccacaact	tgagcatgga	gcattcagct	gtccagcttg	ctataatcaa	tggaagattc	1920
agatggatca	gtttatgcag	cagcttcaaga	gaatggaggc	cctgatttca	aaggctcagg	1980
gtgtgtgatg	agtagtacct	gatacagagc	tggaaggcag	gtgcagcag	gctgagcagg	2040
cccttcagga	cattctgaga	gatgcocaga	tttcagaagg	tgtacagaga	ttccttggtc	2100
tccagtttgc	caaggtgag	agccaagaga	acagctacca	gagccgcctg	gatgacctca	2160
agatgtagtg	ggaaagagtt	cgggctctgt	gaagtccagta	ccagaaccga	gttcgggata	2220
ctcacagagct	catcaactag	atgcagctgc	gcctggcaga	aagtgaagct	ttccttgggaa	2280
acactaacat	ttcctgcctca	gaccactagc	tggggcccaa	tgcttttaaa	agtcctggctc	2340
aggaggccac	aagattagca	gaaagccacg	ttgagtcagc	cagtaaacatg	gagcaactcga	2400
caagggaaac	tgaggactat	tccaacaag	ccctctcact	ggtgcgcga	ggcctgcatg	2460

aaggagtcgg	aagcggaagc	ggtagcccg	acggtgctgt	ggtgcaagg	cttgtgga	2520
aattggagaa	aaccoagtc	ctggcccg	agttgacaag	ggagcgca	acagcgga	2580
ttgaagcaga	taggtcttat	cagcacagtc	tcggcctcct	ggattcagtg	tctcggtctc	2640
agggagtcga	tgatcagtc	tttcaggttg	aagaagcaaa	gaggatcaaa	caaaaagcgg	2700
attcactctc	aagcctggta	accaggcata	tggatgagtt	caagcgtaca	cagaagaatc	2760
tgggaaactg	gaaagaagaa	gcacagcagc	tcttcacagaa	tggaaaaagt	gggagagaga	2820
aatcagatca	gctgctttcc	cgtgcgaatc	ttgctaaaa	cagagcacaa	gaagcactga	2880
gtatgggcaa	tgccactttt	tatgaagtgt	agagcatcct	taaaaacctc	agagagattg	2940
acotgcaggt	ggacaacaga	aaagcagaag	ctgaagaagc	catgaagaga	ctctcctaca	3000
tcagccagaa	ggtttcagat	gccagtgaca	agaccagca	agcagaaaga	gccctgggga	3060
cgctgctg	tgatgcacag	agggcaaaaga	attggggcgg	ggagcgctgt	gaaatctcca	3120
gtgagattga	acaggagatt	gggagttctga	acttggaaagc	caatgtgaca	gcagatggag	3180
ccttggccat	ggaaaaggga	ctggcctctc	tgaagagtga	gatgagggaa	ctggaaaggag	3240
agctggaaa	gaaggagctg	gagtttgaca	cgaatatgga	tgacgtacag	atggttgatta	3300
cagaagccca	gaaggtttgat	accagagcca	agaacgctgg	ggttacaatc	caagcacac	3360
tcaacacatt	agacggcctc	ctgcactctga	tggaccagcc	tctcagtgta	gataaagagg	3420
ggctgtgtct	actggagcag	aagctttccc	gagccaagac	ccagatcaac	agccaactgc	3480
ggcccatgct	gtcagagctg	gaagagaggg	cacgtcacga	gtggggcgcc	ctccatttgc	3540
tgagagacag	catagatggg	attctggctg	atgtgaagaa	cttgagaaac	attagggaca	3600
acotgcccc	aggctgctac	aataccocagg	ctcttgagca	acagtgaagc	tgccataaat	3660
attttccaac	tgaggtttctt	gggatacaga	tctcaggctc	cgaggagccat	gtcatgtgag	3720
tggtgggtat	ggggacattt	gaacatgttt	aatgggttatg	ctcaggtcaa	ctgacctggc	3780
ccattctctg	atcccatggc	caggtggttg	tcttattgca	ccatactcct	tgcttctctga	3840
tgctgggcaa	tgaggcagat	agcactgggt	gtgagaatga	tcaaggatct	ggaccccaaa	3900
gaatagactg	gatggaaaaga	caaaactgcac	aggcagatgt	ttgcctcata	attctgttaa	3960
gtggagactct	ggaatttgga	caagtgtcgt	tgggatatag	tcaacttatt	ctttgagtaa	4020
tgtgactcaa	ggaaaaaact	ttgactttgc	ccaggcatga	aatctctcct	aatgtcagaa	4080
cagagtgcac	cccagtcaca	ctgtggccag	taaaatacta	ttgcctcata	ttgtcctctg	4140
caagctctct	gctgatccaga	gttctcctca	cttacaaccc	aggggtgtgaa	catgtttccc	4200
attttcaagc	tggaagaagt	gagcagtggt	ggagttagga	cctgtaaggc	agggccatcc	4260
agagctatgg	tgcttctgtg	tgccctggcc	cttcaagttc	tggaacctgg	catgacatcc	4320
tttcttttaa	tgatgccatt	gcaacttaga	gattgcattt	ttattaaagc	atttctcacc	4380
agcaaaagca	atgttgggaa	agtatttact	ttttcggtt	caaagtgata	gaaaagtgtg	4440
gcttgggcatt	tgaaaagggt	aaaattctct	agatttatta	gtcctaattc	aatcctactt	4500
ttagaacacc	aaaaatgatg	cgcatcaatg	tattttatct	tattttctca	atctcctctc	4560
tctttcctct	accataata	agagaatgtt	cctactcaca	cttcagctgg	gtcacatcca	4620
tcctctccatt	catccttcca	tcctcttttc	catccattac	ctccatccat	ctctccaaca	4680
tatatattatt	gagtagctac	tgtgtgccag	gggctgggtg	gacagtggtg	acatagtctc	4740
tgccctcata	gagttgattg	tctatgtagg	aagacaagca	tttttaaaaa	ataaatttaa	4800
acttaacaac	ttgtttgttc	acaagtgggt	ttttatgcaa	taaccgcttg	gtttgcaacc	4860
tctttgtcca	acaggaacata	tgttgcaaga	cctcccatcg	ggggcaactg	agttttggca	4920
aggtcgacag	agctctgggt	tgtgcacatt	tctttgcatt	ccagctgtca	ctctgtgcct	4980
ttctacaact	gattgcaaca	gactgttgag	ttatgataac	accagtgggg	attgctggag	5040
gaaccaagag	cacttccacc	ttgctgtggg	agacataggt	gctgccttgc	tctgtatttt	5100
ccttgggaatt	tcttgaaggt	gtttttaaat	aaagacaact	tgttagaaaa	aaaaaa	5156

<210> 131
 <211> 671
 <212> DNA
 <213> Homo sapiens

<400> 131
 aggtctggag ggccacagc cggatgtggg acacogggaa aaagtgtgca tagcacacat 60
 ttttgatcat cggttgcagt gtgtgcaga ttgctgttca cccacactt 120
 cctggggcagc caycagcagg atcatgactc ggaataataa gatgactgtg atccacacct 180
 tcccgatgct ggtggagtgt ttgttgacac ccccgatgaa agtgtgcagc gtcccccaat 240


```

ccattgcgct ggtttatccc tgagtctgt ttccaacgac tgccagtgtt tcagacccaa 300
agaatgaggg caagatccct ctgcgagggg ttccagacct ctctccctac cccactggag 360
tgccatagaag ccaatgggtg cacagtgatg atacgaatgt caattcttgc tccgtcagtg 420
aggatgtcgc ctggaatatt caaattgaat tacagatgca tgaagagggc gtacaagtta 480
gaatttttct ttgccatcac agaaattgtt tagccagatc ttctgtactt cttttccctc 540
cctgaccctt cctgtccccc aggaaggagg gtcagccccc ttgtcaaaac acaggatgcc 600
cgtgacacgg gagacagggt ttcttcacgg acaggaagtg ccttctgggt cctgcacgct 660
ttaactgcta t

```

<210> 132

<211> 590

<212> DNA

<213> Homo sapiens

<400> 132

```

ctgaatggaa aagcttatgg ctctgtgatg atattagtga ccagcggaga tgataagctt 60
cttggcaatt gcttaccacac tgtgtcagc agtgggtcaa caattcactc cattgccctg 120
ggttcatctgt cagcccacaa tctggaggaa ttatcacgtc ttacaggagg tttaaagttc 180
tttgttccag atatatcaaaa ctccaatagc atgattgatg ctttcagtag aatttccctc 240
ggaactgtcgc gaacttttcca gcaacatatt cagcttgaaa gtacagggtg aaatgtcaaa 300
ctccaccatc aattgaaaaa cacagtgaat gtggataata ctgtgggcaa cgacacatgt 360
tttctgattt cgtggcagcg cagtgtgtct cctgagatta tattatttga tctgtatgga 420
cgaaaaatac acacaaataa ttttatcacc aatctaactt ttggacagc tagtcttttg 480
attccaggaa cagctaagcc tgggcactgg acttacaccc tgaacaatac ccatcatctt 540
ctgcaagccc tgaaagtgc agtgacctct cgcgcctcca actcagacct 590

```

<210> 133

<211> 581

<212> DNA

<213> Homo sapiens

<400> 133

```

aggctctgtc cgggggcact gagaactccc tctggaatc ttgggggggt ttggggagag 60
actgtgggccc tggagataaa actgtgtctc totaccacca cctgttacc tagcctgcac 120
ctgtctctcat ctctgcaaa ttccagcttcc ttcccagggt ctctgtgcac tctgtctgtg 180
atgctctggg gagctcatgg gtggaggagt ctccaccaga gggaggctca ggggactggt 240
tgggccaggg atgaatatgt gagggataaa aattgtgtga gagccaaaga attggtagta 300
gggggagaac agagaggagc tgggctatgg gaaatgatt gaataatgga gctgggaata 360
tggtgtgata tctgttacta aaaaagggtc ttttaagaac tacttctcaa tctcttcccc 420
aatccaaacc atagctgtct gtccagtgtc ctcttcctgc ctccagctc ccccaggct 480
ctctctagac tctgtccctg ggctagggca ggggaggagg gagagcaggg ttgggggaga 540
ggctgaggag agtgtgacat gtggggagag gaccagacct c

```

<210> 134

<211> 4797

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 135, 501, 4421, 4467, 4468, 4698

<223> n = A,T,C or G

<400> 134

```

cctgggacca aagtgtgcc cagagctgag ggtcctggag ccacatgaga aggtctctcc 60
ctgtgtacct gtgcagcaca ggttaggggt agtccactga gctgtctagg agaggaccca 120
ggagcagcag agacnccgca agcctttact cataccatat tctgatcctt ttccagcaaa 180
tttgtgtcac taatttgccc cctgaagatc aagatggctc tggggatgac tctgacaact 240

```

tctccggctc	aggtgcaggt	gaggttgta	tgggggcccc	cccccccaa	gacggcaaca	300
gtctacgtcc	gggggcagtg	gtcaggcagt	ctcctgtgtt	tactgagcat	gtactgagtg	360
cacctcgctc	gcoctgtctc	caccacagct	gtcccaaaag	gcaatgctga	ggagaggaat	420
ggggctgtga	gctgtgtgta	aggagagctc	atgcttgga	gtgaggtgaa	ggctgtgagc	480
ccagaagagg	ccagaggcgc	ncctgctccac	gcaggctcat	attcactagg	aatagcttta	540
ctcactaaga	aacctctgga	acccctctca	gaaggttatt	tgaactcctga	gcctctattt	600
tctcatctgc	aaaatcggaa	taataccttg	acctgataag	cttgtggagg	tgtgaaggcg	660
cacagagcca	gctgggggtg	agctcttcca	tccaagctcc	cttctctact	tccctcttcc	720
tgtgtgggact	gggtggagaga	agtcctcgag	ctggagggtg	tcagggaagc	ttccacagag	780
aggtggctct	tgagtgagcc	tcaggaaagag	gggtgagaga	gctaaggaaag	gaggtgtgag	840
tcactccgtg	ggaagtgcac	tagcggaggg	ctgagagctg	caagtgagctg	tatctgttgt	900
tggaaagtgc	tgttgttgga	agtgggggcc	tttttttcaa	ggaggggtgg	gccaggaag	960
tgtgtgcctc	gggataagta	ggataaccac	agtagttatg	ccctaaagg	atgcccaacc	1020
gacctcgtg	gtcacagaaa	agcttccca	gggtggcctag	gcacctgtct	cgtggctcca	1080
gagacagggt	gcacctgaca	cacacaaatg	aaggacagct	ctcctgttcc	attttccaa	1140
gagcttagcc	tccagtgctc	tgtccaggta	ctagcctccc	tcatagctct	agcttgagca	1200
gccacagctc	tctggaggct	cccccgaccc	acccaacaca	ctctgcttct	ggctctcccc	1260
accccccaac	tcccccaact	actctgcttc	tggctctgca	ggtgctttgc	aagataatcc	1320
cttgtccagc	cagaccctct	ccacttggaa	ggacacgcag	ctcctgacga	ctattccccc	1380
gtctccagaa	ccccacggcc	tggaggctac	agctgcctcc	acctccaccc	tgcggctggc	1440
agagggggccc	aaggaggagg	aggtgtgagt	cctgccagaa	gtggagctct	gcctcacccg	1500
ccgggacagc	gagggccaac	cccgaccagc	ggagaccaca	cagctccoga	ccactcaaca	1560
ggcctcaacg	accacagcca	ccacggccca	ggagccccc	acctcccacc	cccacaggga	1620
catgcagcct	ggccaccatg	agacctcaac	ccctgcagga	ccagggcaag	ctgacctcca	1680
cactcccccac	acagaggatg	gaggtccttc	tgcacacgag	agggctgctg	atgtagggag	1740
ctccagctag	ctccacagc	cagagggctc	tggggagcag	gtgagtgccc	tctgcatctc	1800
tggggaattt	gagtggggtg	gtcctaattc	ctggcaactg	gcaggcccta	caacttggcc	1860
ctgcgcgcat	tctgtattct	caccaggaag	acagggcaca	ggggcccgct	tcctccatcc	1920
ccagggcgctc	gcagagcagc	acagactaac	tatgagatca	gagcagaagc	acctctaaag	1980
atcccccaag	agagggctcc	caaaactaca	atccaaactt	gcagccctcg	tccaagagtg	2040
aacgttatac	cagctcattt	atttatagct	tcgtggattt	acgtttacac	taaatagctc	2100
gotatttoata	caaaatgtgt	gctttgtatc	actttttgtg	atatccatgc	catggtccag	2160
ccagggtccg	gagttgatgt	ggcaagaagg	cctggcttcc	ggggccctgt	gcatcctggc	2220
tggggtgcac	ctgagtgggt	ggtggcaaa	atcaggggag	caggagctgc	tctctgggtc	2280
gtagtggagg	tggttgctgc	tgtctggcgt	gaacctggca	acccaatctg	ccccgtccct	2340
ccacaggagc	ttcacctttg	aaacctcggt	ggagaatacg	gctgtagttg	ccgttgagcc	2400
tgaaccgcgc	aaccagctcc	cagtggtatc	gggggcccag	ggggcctcac	agggccctct	2460
ggacaggaaa	gaggtctcgg	gaggtgagtt	ttctttcagg	ggggtagttt	ggggtgaatt	2520
gctgtctgtg	ggcagggtg	gggctgacca	cagccaaagc	cactgtcttt	ggagggctgt	2580
ccagagagcc	caaggagccg	ctgagctgag	ctggccctgt	ctacctgccc	taggggtcat	2640
tgcggggaggc	ctcgtggggc	toatctttgc	tgtgtgcctg	gtgggtttca	tgtctaacgc	2700
catgaagaag	aaggagcaag	gcagctactc	cttggaggag	ccgaataaac	ccaacggcgc	2760
ggcctaccag	aagcccacaca	aacaggagga	attctatggc	tgcacgggga	gccatgcggc	2820
ccctccgccc	tgcacatcac	tagggcccca	cttgctctct	ccttgaaaga	ctcagagccc	2880
tggcctcccc	tgcacacagg	ccacctcccc	agcattccag	ccctctgggt	cgctctggcc	2940
cacggagtg	tgggtgtgct	gggagctcca	ctctgcttct	ctgactctgt	ccctggagat	3000
tagggaccaca	ggggtttctc	gcataggacc	tttccaacc	ccagcagacc	tggcatcgca	3060
ccattctgac	tgggtttctc	caaaactgaag	cagctctccc	ccaggtccag	ctctggagg	3120
gagggggatc	ggcgtctctt	ggacctaaat	ggcctcatgt	ggctgggggc	tccctggggt	3180
ggggcttggtg	gctcacacac	ctgtagcact	tactggttag	accaagcatc	tgtgggggtg	3240
ggccgctgag	tggcagggga	caggagtcac	tttgtttgct	ggggaggtct	aatctagata	3300
tcgacttgtt	tttcacatg	tttccctcag	ttctttgttc	atagcccagt	agacctgtt	3360
actcttgagg	taagttaagt	aagttgattc	ggatatcccc	catcttgctt	ccctaattca	3420
tgttcggagg	acagcatcag	ggttaagaag	actttttttt	ttttttttta	ttagagagaa	3480
ccaaatctgc	aagccaaaat	gtaggcttag	tttgtgtgtt	gtctcttgag	tttgtcgctc	3540
atgtgtgcac	cagggtatgg	actatctgtc	tgtgtggccc	ttctgtgtgc	tctgttggga	3600
ggctggccag	tcaggctgc	cgtggggccc	ccgctctctt	caagcagctg	tgcctgtgtc	3660
catgcgctca	gggcatgtct	gaggcctggg	ccgtgccacc	gttgaggag	cccgctgtag	3720

aagtgaatgc	tgggactcag	octtcagaca	gagaggactg	tagggagggc	ggcagggggc	3780
tggagatcct	ctcgaggctc	cacgcccgct	ctcctgtggc	gccgtctcca	ggggctgctt	3840
ctctctggaa	attgacgagg	gggtgtcttg	cgacgagctg	ctctgagcgc	ctccatccaa	3900
ggccaggttc	tcctgtagct	ctctgtggcc	caacctgggc	ctctggcttg	aatcagggaat	3960
attttccaaa	gagtgatagt	cttttgcctt	tggcaaaact	ctacttaate	caatgggttt	4020
ttccctgtac	agtagatatt	ccaaaatgt	taaaacttta	tataaagtag	tctgtgaagt	4080
ccactgcctt	cgcttcttgc	ctctgtgctg	tgtgtgaact	gacccgaact	ttctgcaaac	4140
accaacatgt	tgggaaactt	ggctcgaaat	ctctgtgctt	cgcttcttcc	atggggaggg	4200
attctgggtc	cagggtccct	ctgtgtatct	tttggctgaa	tttggctgaa	attctcaggt	4260
aggctcgtag	gttcagccaa	ggttttataa	ggctgatgtc	aattctctgt	tggccaagct	4320
ccaagccat	cttctaaatg	gcaaaggaa	gtggatggcc	ccagcagcgc	tgtccatctg	4380
cgctgtgtca	cagcggaggt	gtggagccga	ggctacccoc	ncagacacoc	tggacatcct	4440
ctctccaccc	ggctcgagag	gcaaanncc	agcccagggt	ctcgcaacta	cttctgtatt	4500
tgacaacggt	tcagcgactc	cgttggccac	tcogagagtg	ggccagtgct	tggatcaagag	4560
atgacacccc	aagccaaagg	aacctgtgtc	cgttatctga	tactgcgact	ttctgcccgt	4620
agtgtagtac	tgacatagac	tcgggggtgc	ggaaaagggt	cggtcgacca	tgtccatctg	4680
tggttcctgt	ggacggtacc	caagccagag	gtgggttcat	ttgtgtaacg	acaaataaag	4740
gtactgtgca	tttcggggcaa	cggctgctgt	ggtgggtggt	gagtctcttc	ttggcctc	4797

<210> 135

<211> 2856

<212> DNA

<213> Homo sapiens

<400> 135

tagtcgcggg	ttccccgagt	agcagcgccg	ggagcaggag	acaaaacgac	gggggtcgga	60
ctgaagagtc	cagtgaggag	cccgggacgc	gagcacgagc	ctgagcggga	gagcgcgcgt	120
ggcagccccc	tcgccaccgc	cgtacccgcg	cgacccagag	ccaccagcgc	agcgctgcga	180
tggagccccc	cagcaagaag	ctgacgggtc	ggctcatgct	ggctgtggga	ggagcagctg	240
ttggctccct	cgactttggc	tacaaactgt	gagtcataaa	tgccccccag	aaggtgatgc	300
aggagtctca	caacagacac	tgggtccaac	gcatgtggga	gagcatccgt	cccacacagc	360
tcacccagct	ctggctccct	tcagtgccca	ttttttctgt	tgggggcgat	attggctcct	420
ttctgtgtgg	octtttcgct	aaccgctttg	gcggcgccaa	ttcaatgctg	atgatgaacc	480
tgtctggcct	cgtgtccccc	gtgctcatgg	gcttctogaa	actggggcaag	tcctttgaga	540
tgdtgatctc	ggggcgcttc	atcatcggtg	tgtactgcgg	cctgaccaca	ggctttogtc	600
ccatgtatgt	gggtgaagt	tcacccacag	octttcgtgg	ggccctgggc	accctgcacc	660
agctggggat	cgtcgtgggc	atcctcatcg	cccaggtgtt	ogggcctggc	tcocatcatg	720
gcaacaagga	cctgtggccc	ctgctgctga	gcatactctt	oatcccgccc	ctgctgcagt	780
gcactgtgtc	gcccttctgc	cccagagatc	cccgttctct	gtctcaatac	cgcaacaggg	840
agaaaggggc	caagagctgt	ctaagaagc	tgcgcgggac	agctgacgtg	accatgaacc	900
tgacaggagat	gaagggaag	agtcggcaga	tgatgcggga	gaagaaggtc	accatcctgt	960
agctgttccg	ctcccccgcg	taccggccag	ccatctctac	cgctgtgggt	ctgcgactgt	1020
cccagagact	gtctggcacc	aacgctgtct	ttatattact	ccagagcact	ttcgagaagg	1080
oggggggtgca	gcagcctgtg	tatgcacaca	ttggctccgg	tatgttaaac	accgctctca	1140
ctgtctgtgt	gctgttttgt	gtggagcgag	caggccgggc	gacctgcac	ctcataggcc	1200
tcgctggcat	ggcgggttgt	gccaactact	tgacactcgc	gtatgacatg	ctggagcagc	1260
taccctggat	gtctctatct	agcatcgttg	ccatctttgg	ctttgtggcc	ttctttgaag	1320
tgggtccctg	ccccctacca	tggttcatcg	tggctgaact	ctttagccag	ggctccagct	1380
cagctggcat	tcgcgttgca	ggcttctcca	actggacctc	aaatttcaat	tggggcagtg	1440
gcttccagta	tgtggagcaa	ctgtgtggct	cctacgtctt	catcatcttc	actgtgctcc	1500
tggttctgtt	cttcaacttc	acctacttca	aagtctctga	gactaaaggc	cggcactctg	1560
atgagatgca	tttcggcttc	cggcaggggg	aagtgtataa	aaagtgcaga	acaccggagc	1620
agctgttcca	ttccctgtgg	gctgattccc	aagtgtgagt	cgccccagat	caccagcccg	1680
gcctgtctcc	agcagcccca	aggatctctc	aggagcagac	gcagctggct	gagacttcca	1740
aacctgcagc	atgtcagccg	agccgggccc	ggggctccct	ttctcagcca	gcaatgatgt	1800
ccagaagaat	attcaggact	taacggctcc	aggattttaa	caaaagcaat	actgtgtgct	1860
aaatctattc	agacaagcaa	caggttttat	aattttttta	ttactgattt	tgttattttt	1920
atatacgctc	gagtctcctg	tgccacatc	ccaggcttca	cctggaatgg	ttccatgcct	1980

gaggggtggag	actaagccct	gtcgagacac	ttgccttctt	caccageta	atctgtagg	2040
ctggacctat	gtcctaagga	cacactaatc	gaactatgaa	ctacaaagct	tctatccag	2100
gaggtggcta	tggccacccg	ttctgtctggc	ctggatctcc	ccactctagg	ggtagagctc	2160
cattaggatt	tgccccttcc	catctcttcc	tacccaacca	ctcaaatata	tctttcttta	2220
cctgagacca	gttgggagca	ctggagtgca	gggaggagag	gggaagggcc	agtctgggct	2280
gcggggttct	agtctccttt	gcactgaggg	ccacactatt	accatgagaa	gagggcctgt	2340
gggagcctgc	aaactcaactg	ctcaagaaga	catggagact	cctgcctgt	tgtgtataga	2400
tgcaagatat	ttatatatat	ttttggttgt	caatatataa	tacagacact	aagtatatgt	2460
atatctggac	agcccaactt	gtaaatatcac	cacctcactc	ctgttactta	cttaaacaga	2520
tataaatggc	tggttttttag	aaacatggtt	ttgaaatgct	tgtggattga	gggtaggagg	2580
tttggatggg	agtggagacag	aagttaagtgg	ggttgcaacc	actgcaacgg	cttagacttc	2640
gactcaagat	ccagtcctctt	acacgtacct	ctcatcagtg	tctcttctgt	caaaaaatctg	2700
tttgatccct	gttaccacga	gaatatatac	attottttatc	ttgacattca	agggatttct	2760
atcacatatt	tgatagttgg	tgttcaaaaa	aacactagtt	ttgtgccagc	cgtgatgctc	2820
aggcttgaaa	tcgcattatt	ttgaatgtga	agggaa			2880

<210> 136

<211> 356

<212> DNA

<213> Homo sapiens

<400> 136

ggtggagcca	aatgaagaaa	atgaagatga	aagagacaga	cacctcagtt	tttctggatc	60
agggcatgat	gatgatgaag	attttatctc	cagcaccatt	tcaaccacac	cacgggcttt	120
tgaccacaca	aaacagaacc	aggactggac	ctagtggaa	ccaagccatt	caaatccgga	180
agtgctactt	cagacaaaca	caaggatgac	tgatgtagac	agaataggca	ccactgctta	240
tgaaggaaac	tggaaaccag	aagcacaccc	ctccctcatt	caccatgagc	atcatgagga	300
agaagagacc	ccacattcta	caagcacaat	caggccaact	cctagtagta	caacg	356

<210> 137

<211> 356

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 254, 264, 279, 281, 290, 328, 342

<223> n = A,T,C or G

<400> 137

gcagggtggag	aagacatttt	attgttctctg	gggtctcttgg	aggcccatgg	gtggggcttg	60
gtcactggct	gcccccgga	caggcgctg	ctccatggct	ctgcttctgg	tagtctgtgg	120
ctatgtctcc	cagcaaggac	agaaactcag	aaaaatcaat	cttcttatcc	tcattcttgt	180
cccttttttc	aaagacatcg	gcgaggtaat	ttgtgccttt	tttactctgg	cccgcgacca	240
cgctaaggcc	aanantccag	acanaayggcc	gggcgggtnc	nataggggan	cccaacttgg	300
ggaccacaac	tctggcgctg	aaacacang	gcataagctt	gnttctctgt	gggaaa	356

<210> 138

<211> 353

<212> DNA

<213> Homo sapiens

<400> 138

aggtccagtc	ctccacttgg	cctgatgaga	gtggggagtg	gcaaggagac	tttctctctg	60
aatagacact	tagattttct	tcttctggga	agaaaccacc	tgtccatcca	ctgactcttc	120
tacatctgat	tgaaatttgc	tgctgtctac	accacctctc	gaagaggctt	ccctgatgcc	180
aatgccagcc	atcttggcat	cctggccctc	gagcaggctg	cggttaagtag	cgtatctctg	240
ctccagccgt	gtctttatgt	caagcagcat	cttgtactcc	tggttctgag	cctccatctc	300

gcactggagc tcaactcagac ctgcscgsg mssmcgctam gccgaattcc agc 353

<210> 139

<211> 371

<212> DNA

<213> Homo sapiens

<400> 139

agcgtggtcg cgcccgaggt ccatccgaag caagattgca gatggcagtg tgaagagaga 60
 agacataatt tacacttcaa agctttggtg caattcccat ogaccagagt tggctccgacc 120
 agccttggaa aggtcactga aaaatcttca attggattat gttgacotct accttattca 180
 ttttccagtg totgtaaaag caggtgagga agtgatccca aaagatgaaa atggaaaaat 240
 actatttgac acagtggatc tctgtgccac gtgggaggcc gtggagaagt gtaaaagatgc 300
 aggattggac ctgcccgggc ggcgctcga aagccgaatt ccagcacact ggcggccggtt 360
 actagtggat c 371

<210> 140

<211> 370

<212> DNA

<213> Homo sapiens

<400> 140

tagcgtggtc gcggccgaggt tcatctctcc tttgggaact agggggctgc tgggtgggaaa 60
 tgggagccag ggcagatggt gcatctcctt gtgtccctgt aaatgtggga ctacaagaag 120
 aggagctgcc tgaagtggatc tttctcttcc tggtaactct ctggcccagc ctcatggcag 180
 aatagaggta tttttaggct atttttgtta tatggctctt ggtcaaaatc cctgtgtagc 240
 tgaattccca agccctgcat tgtacagccc cccactcccc tcaccaccta ataaaggaat 300
 agttaacact caaaaaaaa aaaaaacctg cccgggcggc cgctcgaaa cgaatttcca 360
 gcacactggc 370

<210> 141

<211> 371

<212> DNA

<213> Homo sapiens

<400> 141

tagcgtggtc gcggccgaggt tcctctgtgc tgcctgtcac agcccgatgg taccagcgca 60
 ggtgtgagc agtgccagag cctcatcca gtggcaggga acaggggtca tcaactatccc 120
 aaggagcttc agggctcctgg tactcctcca cagaatactc ggagtattca gactaactcat 180
 catctccagg ggttaccocg tcttctcctc ctgcatgaga gacgcggagc acaggcacag 240
 catggagctg ggagccggca gtgtctgcag cataactagg gaggggtcgt gatccagatg 300
 cgatgaactg gccctggcag gcacagtgtc gactcatctc ttggcgacct gccggggcgg 360
 ccgctcgaag c 371

<210> 142

<211> 343

<212> DNA

<213> Homo sapiens

<400> 142

gogtttttag gccaatggtg taaaaggaaa tatcttcaca taaaaactag atggaagcat 60
 tgtcagaaac ctctttgtga tgtttgtctt caactcacag agttgaacat tctttttcat 120
 agagcagttt tgaaacactc ttttttagaa tttgcaacgc gatgattgga tctgtatgag 180
 gtcctcatgt gaaacgggat acctttacat aaaaactaga cagtagcatt ctacagaaatt 240
 tctttgggat gtgggcatc aaccacaga ggagaacttc atttgataga gcagttttga 300
 aacacccttt ttgtagaatc tacaggtgga catttagagt gct 343

<210> 143

<211> 354
 <212> DNA
 <213> Homo sapiens

<400> 143
 aggtctgatg gcagaaaaac tcagactgtc tgcaacttta cagatgggtgc attgggttcag 60
 catcaggagt gggatgggaa ggaaagcaca ataacaaaga aattgaaaaga tgggaaatta 120
 gtgggtgagtg gtgtcatgaa caatgtcacc tgtactcgga tctatgaaaa agtgagaataa 180
 aaattccatc atcacttttg acaggagtta attaagagaa tgaccaagct cagttcaatg 240
 agcaaatctc catactgttt ctttcttttt tttttcatta ctgtgttcaa ttatctttat 300
 cataaacatt ttacatgcag ctatttcaaa gtgtgttga ttaattagga tcatt 354

<210> 144
 <211> 353
 <212> DNA
 <213> Homo sapiens

<400> 144
 ggtcaaggac ctggggggacc ccaggtcca gcagccacat gattctgcag cagacaggga 60
 cctagagcac atctggatct cagcccaacc cctggcaacc tgctgccta gagaactccc 120
 aagatgcagc actaagttag attctgccat ttagaataat tctggatccc tggggctgtg 180
 gttaagttag ttaactttca ttctgttcta cgatagtctt cagaggtggg aacagatgaa 240
 gaaaccatgc ccagagaga gttaagtgc ttctcttcta tggagccagt gttccaaact 300
 aggtttgctt gataccagac ctgtggcccc acctcccatg cagggtctctg tgg 353

<210> 145
 <211> 371
 <212> DNA
 <213> Homo sapiens

<400> 145
 cagggtctgc ataaactggg ctggagtttc tgacgactcc ttgttcacca aatgcacat 60
 ttctgtgagc ttgtctggcc ctccgttgag tccacttggc ttctgtctcc ccacagctcc 120
 attgccaact ttgatcaacta gctttttctt ctgcccacac ctctctcgac ttgttgactgc 180
 aatgcacact gcaagaatca aagccaaggc caagagggat gccaaagtga tcagccattc 240
 tggaaatttg ggtgtcctta taggaccaga ggtgtgtgtt gctccacott ctgtactccc 300
 atgtgagacc tcggccgcga ccacgctaag ccgaattcca gcactctggc ggcccgttac 360
 tagtggatcc g 371

<210> 146
 <211> 355
 <212> DNA
 <213> Homo sapiens

<400> 146
 ggtctctcgt cctettocca gaggtgtcgg ggcttggccc cagcctccat ctctgtctct 60
 caggatggcg agtagcagcg gctccaaggc tgaattoatt gtggaggga aatataaact 120
 ggtacgggaag atcgggtctg gctccttcgg ggacatctat ttggcgatca acatcaacaa 180
 cggcgaggaa gtggcagtgga agctagaatc tcagaaggcc aggcacatccc agttgtctga 240
 cgagagcaag ctctataaga ttcttcaagg tggggtttggc atccccaca taagggtgga 300
 tggtcaggaa aaagactaca atgtactagt catggatctt ctgggacctc gctc 355

<210> 147
 <211> 355
 <212> DNA
 <213> Homo sapiens

<400> 147

```

ggctctgttac  aaaaatgaaga  cagacaacac  aacattttact  ctgtggagat  atcctactca  60
tactatgcac  gtgctgtgat  tttgaacata  actcgtccca  aaaacttgto  acgatcatcc  120
tgacttttta  ggttggctga  tccatcaatc  ttgcaactca  ctgtttacttc  tttccagatg  180
ttgttaggag  caaagctgac  ctgaacagca  accaatgggt  gtgatatacc  aacatgcagt  240
ttttcccat  aatatggaa  atattttaag  tctatcatcc  cattatgagg  ataaactgct  300
acatttggt  tatcttcatt  ctttgaacaa  caatctatcc  ttggcaactcc  ttacg  355

```

<210> 148

<211> 369

<212> DNA

<213> Homo sapiens

<400> 148

```

aggctctctcc  cccctctctcc  ctctctctgcc  agccaagtga  agacatgctt  acttcccctt  60
caccttctctt  catgatgtgg  gaagagtgtct  gcaacccagc  cctagccaac  accgcatgag  120
agggagtggtg  ccgaggggctt  ctgagaaggt  ttctctcaca  tctagaaga  agcgcttaag  180
atgtggcagc  cctctctctt  caagtggctc  ttgtctgttt  gccctgggag  ttctcaaat  240
gctgcagcag  cctccatcca  gccctaggat  gacatcaata  cacagaggaa  gaagagtcatg  300
gaaaagatga  gagaagttac  agactctcct  gggcgacccc  gagagcttac  cattctctcag  360
acttctcca  369

```

<210> 149

<211> 620

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 169, 171, 222, 472, 528, 559, 599

<223> n = A,T,C or G

<400> 149

```

actagtcaaa  aatgctaaaa  taatttggga  gaaaatattt  ttaagttagt  gttatagttt  60
catgtttatc  tttttattatg  ttttgtgaag  ttgtgtcttt  tcaactaatta  cctatactat  120
gccaatattt  ccttatatct  atccataaaca  tttatactac  atttgaana  naatatgcac  180
gtgaaactta  acactttata  aggtaaaaat  gaggtttcca  anatttaata  atctgatcaa  240
gttcttgtaa  tttccaaata  gaatggactt  ggtctgttaa  gggctaagga  gaagagggaag  300
ataagggttaa  aagttgttaa  tgaccaaaaca  ttctaaaaga  aatgcacaaa  aaaagtttat  360
tttcaagcct  tcgaactatt  taaggaaagc  aaaatcattt  cctaaatgca  tatcatttgt  420
gagaatttct  cattaatatc  ctgaatcatt  catcttcaata  aggcctatgt  tnaactcgat  480
atgtctctaa  gaaagtacta  tttcatggct  caaacctggt  tgccatantt  gggtaaaggc  540
ttccctctaa  gtgtgaaatt  atttaaaatg  aaattttctt  ctttttaaaa  attctttana  600
agggttaagg  gtgttgggga  620

```

<210> 150

<211> 371

<212> DNA

<213> Homo sapiens

<400> 150

```

ggtccgatca  aaacotgcta  cctcccacag  actttactag  tgccgataaa  ctttctcaaa  60
gagcaaccag  tatcacttcc  ctgtttataa  aacctctaac  catctcttgg  ttctttgaac  120
atgctgaaaa  ccacotggct  tgcgatgtat  cccgaatttg  yaattctttt  ctctcaaatg  180
aaaatttaat  ttttagggatt  catttctata  ttttcacata  tgtagtatta  ttatttcttt  240
atatgtgtaa  ggtgaaattt  atggattttg  agtgtgcaag  aaaatatatt  tttaaagcct  300
tcatttttcc  ccagtgaaat  gatttagaat  tttttatgta  aatatacaga  atgttttttc  360
ttacttttat  a  371

```

<210> 151

<211> 4655

<212> DNA

<213> Homo sapiens

<400> 151

```

gggaacttgag  ttctgtttatc  ttcttaagta  gattcatatt  gtaagggtct  cgggggtggg  60
gggttggcaca  aatcctggag  ccagaagaaa  ggacagcagc  attgatcaat  ctctacagcta  120
acatgttgtag  cctggaaaac  aatgccocaga  ctcaatttag  tgagccacag  tacaagcaacc  180
tggggctcctt  gaacacgatg  gaccagocaga  ttccagaacgg  ctccctcgctc  accagctccct  240
ataacacagca  cacocgcgag  aacagocgtca  cggcgccctc  gcctctacgca  cagccocagct  300
ccacctcttga  tctctctctc  coactcaoccg  coactccctc  caacacccgac  taccocaggcc  360
cgcaacgtttt  cgaagtgtcc  ttccagcagt  cgagcacccg  caagtccggc  accctggagct  420
attccactga  actgaagaaa  ctctactgcc  aaattgcaaa  gacatgcgac  atccagatca  480
agggtgatgac  cccacctcct  cagggagctg  ttatccgcgc  catgcctgtc  tacaaaaagg  540
ctgaagcacgt  caccggaggt  gtgaagcggt  tgactccgag  tgagctgagc  cgtgaattca  600
acgaggggaca  gattgcccc  yctagtcatt  tgattcgagt  agagggggaac  agccatgccc  660
agtatgttaga  agatcccatc  acaggaagac  agagtgtgct  ggtaccttat  gagccacccc  720
aggttggcac  tgaattcacg  acagtcttgt  acaatttcat  gtgtaacagc  agttgtgttg  780
gaggagttaga  cgcgcgtcca  attttaatca  ttgttactct  ggaacccaga  gatgggcaag  840
tctctggccg  acgctgcttt  gaggcccgga  tctgtgcttg  ccaggaaga  gacaggaaag  900
cgagtgaaga  tagcatcaga  aagcagcaag  ttccggacag  tacaagaac  ggtgatggtt  960
cgaagcgccc  gttctgctcag  aacacacatg  gtatccagat  gacatccatc  aagaaacgaa  1020
tgatccccaga  tgatgaactg  gtatacttac  cagtgaaggg  ccgtgagact  tatgaaatgc  1080
tggtgaagat  caaagagtc  ctggaaactca  tgcagtacct  tcttcagcac  acaattgaaa  1140
cgtaacaggca  acagcaaacg  cagcagcacc  agcacttact  tcagaaacag  accctaatca  1200
agctcccatc  ttcatcttgt  aacagctccc  caaccttgaa  caaaatgaa  agcatgaaca  1260
agctcctctc  tgtgagccag  cttaaccaacc  ctacagcagc  caagccctc  actcctacaa  1320
ccattctga  tggcatggga  gccaacattc  ccatgatggg  ccaccaatg  caatggcgtg  1380
gagacatgaa  tggactcagc  cccacccagg  cactccctcc  cccactctcc  atgcatcca  1440
ctcccatc  caccaccoca  cctccgtatc  ccacagattg  cagctttgtc  agtttcttgc  1500
cgaggttggg  ctgttcatca  tgtctggact  atttccagac  ccaggggctg  accaccatct  1560
atcagattga  gcattactcc  atggatgac  tggcaagtct  gaaaaatccc  gagcaatttc  1620
gacatgcgat  ctggaagggc  atcctggacc  acoggcagct  ccacgaattc  tctccctctt  1680
ctcatctcct  gcggaaccca  agcagtgcc  ctacagtca  tgtgggctcc  agtgagacc  1740
ggggtgagcg  tgttattgat  gctgtgogat  tcacccctcg  ccagaccatc  tctttccac  1800
ccagagatga  gtggaatgac  ttcaactttg  acatggatgc  tcggccgaat  aagcaacagc  1860
gcatacaaga  ggagggggag  tgagcctcac  oatgtgagct  ctctctatcc  ctctcctaac  1920
tgccagcccc  ctaaaagcac  tctctgctaa  tcttcaaaagc  ctctccctca  gctcctcccc  1980
ttcctcttgt  ctgatttctt  aggggaagga  gaagtaagag  gcttacttgc  taacctaac  2040
atctgacctg  gcactcaatt  ctgattctcg  cttaaagcct  tcaaaactat  agcttgacga  2100
ctcagtagctt  gccatggcta  ggtgaagtg  agcaaaaaag  agttgggtgt  ctccctaaag  2160
tgcaagagatt  tctcatggac  ttttataaag  ctctatagct  ctctatagct  aagactatat  2220
atataaatgt  ataaatatac  agtatagatt  ttgggtggg  gggcattgag  tatgttttaa  2280
aatgttaatt  aatgtaaaag  aaattgagtt  gcacttattg  accatttttt  atattacttg  2340
ttttggatgt  ctgtctcata  ctcttccct  taagggggat  catgtatggt  gataggctac  2400
tagagcttaa  tgcatactgt  gagtgaogat  gatgtacaga  ttcttctagt  ctgtgtgatt  2460
ctaaatcat  gccacatcaa  acccttgagt  agatccatt  ccattgctta  ttatgtaggt  2520
aagactgtag  alatgtattc  tttctcagt  ttgtgtatat  ttatattac  tgaacttatc  2580
tctagtgtat  atgggtccag  ttgggggtgat  ttaattccagt  tataagaaga  agttcatgtc  2640
caaacgctcct  ctttagtttt  tgggtgggaa  tgaggaataa  tcttaaaagg  cccatagcag  2700
ccagttcaaa  aacaccgcac  gtcattgatt  tgagcatcat  acttaacccc  taaattttaa  2760
taccagatca  cttactctac  aatattgatt  gggaaaaaat  ttgctgcgat  tacagaggtt  2820
ttaaaactaa  atttccactac  tagattgact  aactcaaat  cacatttgct  actggtgtaa  2880
gaattctgat  tgatttgatt  gggatgaatg  catctctatc  agttctaaac  gtgaagtttt  2940
actgtctatt  aatattcagg  gtaaatagga  atccatcaga  atgttgtagt  ctgtactaaa  3000
cagtaagata  tctcaatgaa  ccataaattc  aactttgtaa  aaacttttg  aagcatagat  3060
aatattgttt  ggtaaatgtt  tcttttgttt  ggtaaatgtt  tcytttaaag  accctcctat  3120

```



```

tctataaaac tctgcatgta gaggettgtt tacctttctc tctctaaagg ttacaatagg 3180
agttgggtgatt tgaaaaatat aaaattatga gatttggttt cctgtggcat aaattgcac 3240
actgtatcat tttctttttt aaccggtaag agtttcagtt tgttggaagg taactgtgag 3300
aaccacggtt ccgctccatc tcccttaggg actaccata gacatgaagg gtccccaag 3360
agcaagagat aagtctttca tggctgctgt tgcttaaac acttaacga agagttccct 3420
tgaaaacttg ggaacaacatg ttaaagacaa tatccagat ctttcagaaa tataacacat 3480
ttttttgcat gcatgcaaat gagctctgaa atcttccat gcattctgtt caagggtcgt 3540
cattgcacat aagcttccat ttaattttta aagtgcataa gggccagcgt ggctctaaaa 3600
ggtaagtgtt ggattgcctc tgaaaagtgt gtatatattt tgtgtgaaat tgcatacttt 3660
gtattttgat tatttttttt ttcttcttgg gatagtggga ttccagaaac cacacttgaa 3720
accttttttt atogtttttt tattttcatg aaaataccat ttagtaagaa taccacatca 3780
aataagaatt aatgctacaa ttttaagagg ggagggaagg gaaagttttt ttttttatta 3840
tttttttaaa attttgtatg ttaaagagaa tgagtccctg atttcaaatg tttgtgtgac 3900
ttaaatggta ataagcactg taaacttctg caacaagcat gcagctttgc aaacccatta 3960
aggggaagaa tgaaagctgt tccttggtcc tagtaagaag acaaaactgt tocccttact 4020
tgctaggggt ttgaataaac ctaggacttc cgagctatgt cactactatt caggtaacac 4080
tagggccttg gaaatccctg tactgtgtct catggatttg gcactagcca aagcgaggca 4140
cccttactg gcttacctcc tcaatggcagc ctactctcct tgagtgtatg agtagccagg 4200
gtaaggggta aaaggatagt aagcatagaa accactagaa agtgggctta atggagtctt 4260
tgtggcctca gctcaatgca gttagctgaa gaattgaaaa gttttgtttt ggagacgttt 4320
ataaacagaa atggaagaca gagttttcat taaactcctt tacctttttt ttttcttgt 4380
aatccctcaa aataacagta tgtgggatat tgaatgttaa agggatattt ttttctatta 4440
tttttataat tgtacaaaat taagcaaatg ttaaagttt tatatgtctt attaatgttt 4500
tcaaaaagga ttatacatgt gatacathtt ttaagcttca gttgcttgtc ttctgtgact 4560
ttctgttatg ggcttttggg gagccagaag ccaatctaca atctcttttt gtttgccagg 4620
acatgcaata aaattttaaa aataataaaa aacta 4655

```

<210> 152

<211> 586

<212> PRT

<213> Homo sapiens

<400> 152

```

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
1 5 10 15
Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
20 25 30
Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
35 40 45
Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
50 55 60
Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
65 70 75 80
His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
85 90 95
Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
100 105 110
Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Gln Gly
115 120 125
Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
130 135 140
Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
145 150 155 160
Glu Gly Gln Ile Ala Pro Ser Ser His Leu Ile Arg Val Glu Gly Asn
165 170 175
Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
180 185 190
Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Val

```

195	200	205
Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg		
210	215	220
Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val		
225	230	235
Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg		240
	245	250
Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp		255
	260	265
Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr		270
	275	280
His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp		285
	290	295
Glu Leu Val Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu		300
305	310	315
Val Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Leu Gln His		320
	325	330
Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu		335
	340	345
Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser		350
	355	360
Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val		365
	370	375
Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr		380
385	390	395
Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met		400
	405	410
Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro		415
	420	425
Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro Pro		430
	435	440
Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys		445
	450	455
Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr		460
465	470	475
Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro		480
	485	490
Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln		495
	500	505
Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser		510
	515	520
Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val		525
	530	535
Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro		540
545	550	555
Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn		560
	565	570
Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu		575
	580	585

<210> 153

<211> 2007

<212> DNA

<213> Homo sapiens

<400> 153

gaattcgtcg ctgctccagg gaaagtctgt ttactccact gactctctct tttcctgata 60

acatggccag	caagaaagta	attacagtgt	ttggagcaac	aggagctcaa	ggtggctctg	120
tggccaggcg	aattttggag	agcaaaaaat	ttgcagttag	agcagtgcac	agggatgtga	180
cttgaccaaa	tgccctggag	ctccagcgcc	ttggagctga	ggtggctcaa	ggtgacctga	240
atgataaaag	atcgggtggag	agtgccttaa	aaggtgtcta	tggggccttc	ttggtgacca	300
actctctggga	ccctctcaac	caagataaag	aagttgtctg	ggggaagctg	gtggcagact	360
ccgcgcaagca	ctcgggtctg	aagcacgtgg	tgtacacggy	cctggagaac	gtcaagcgac	420
tgacggatgg	caagctggag	gtgccgcact	ttgacagcaa	gggcgagggt	gaggagtact	480
tctggtccat	tggcatcccc	atgaccagtg	tccgcgtggc	ggcctacttt	gaaaaacttc	540
tccggagctgt	gcggcccggt	aaagcctctg	atggagatta	ctacacottg	gctgtaccga	600
tgaggagctgt	accaatggat	ggtatctctg	ttgctgatat	tggaagcagc	gtctctagca	660
tttttaattc	cccaaggaa	tttttaggca	aggccgtggg	gctcagtcca	gaagcactaa	720
caatacagca	atatgctgat	gttttgccta	aggctttggg	gaaagaagtc	cgagatgcaa	780
agattacccc	ggaagcttct	gagaagctgg	gattccctgc	agcaaaaggaa	atagccaata	840
tgtgtcgttt	ctatgaaatg	aagccagacc	gagatgtcaa	tctcaccac	caactaaatc	900
ccaaagtcaa	aagcttcagc	cagtttatct	cagagaacca	gggagccttc	aagggcactgt	960
agaaaaatag	ctgttccagt	aggcctctgc	accacacagc	ctctttctct	cttgatcctt	1020
ttctcttcta	cggcacacaa	ttcatgttga	cagaacatgc	tggaatgcaa	ttgtttgcaa	1080
caccgaagga	tttctcggg	tgcctctctc	agtaggaagc	actgcattgg	tgataggaca	1140
cggaattttg	attcacattt	aacttgtctg	ttagtataaa	gggtgtgtaca	actgttttgt	1200
aaaaatgagaa	gcctcggaa	ttggagcttc	tctctacca	ctaatgggag	gcgagattat	1260
aactgggattt	ctcctgggtg	agtaatttca	agccctaagt	ctgaataatc	cctagcgagc	1320
tccagttttc	tcaactgcac	tgcaaaattc	ccagtgaact	tttaagtaact	tttaacttaa	1380
aaaaatgaac	atctttgtag	agaattttct	ggggaacatg	gtgttcaatg	aacaagcaaa	1440
agcatgggaa	atgctaaaa	tcagttttgc	ctcaagattg	gaagtttat	ttctgaactca	1500
ttcatgaaag	catcatattg	gccacatttc	aattatctat	ctatttaatt	cttgatcctt	1560
cattttatcca	ttctgcaaac	ttttcttgag	caccagcagc	ggtggccatt	tttggaacttc	1620
tcttcattcc	tatgtgtttt	cttatcaaa	tgtatccact	tcgaaggctt	cccttccagt	1680
ctgtggttgt	gttcaagtca	tgccagggcc	agggggccca	tctcctcgtt	tagctctagg	1740
caaaatccag	gggatctcca	gtggggagcg	ggggcgagaa	gctggaggga	agggcctgtga	1800
agggttaggca	tgtggaaa	caagggtgaca	gaaggcccca	ataggacctt	tctatatctc	1860
tggcttagca	ttttctacat	catattgtaa	tcgtcttatt	tgctagtttt	cttccctaac	1920
gtgagtgaact	aacagtcact	tttatccag	tgccgtgtac	ataataagtg	atcaataaat	1980
gttgattgac	taaaaaaaaa	aaaaaaaa				2007

<210> 154

<211> 2148

<212> DNA

<213> Homo sapiens

<400> 154

gaattcgtgc	ctgctccagg	gaaagtcttg	ttactccact	gactctctct	tttctcgata	60
acatggccag	caagaaagta	attacagtgt	ttggagcaac	aggagctcaa	ggtggctctg	120
tggccaggcg	aattttggag	agcaaaaaat	ttgcagttag	agcagtgcac	agggatgtga	180
cttgaccaaa	tgccctggag	ctccagcgcc	ttggagctga	ggtggctcaa	ggtgacctga	240
atgataaaag	atcgggtggag	agtgccttaa	aaggggaaag	tggtggcaca	ctccgccaag	300
cacctggggtc	tgaagcacgt	ggtgtacacg	ggcctggaga	actgaacgag	actgaaggat	360
ggcaagctgtg	aggtgcccga	ctttgacacg	aagggcgagg	tgaggagcta	ctcttggtcc	420
attggcatcc	ccatgaccag	tgtccgctgt	gcggcctact	ttgaaaactt	tctcggggcg	480
tggcgccccc	tgaagccctc	tgtatggagat	tactaacctt	tggtcttacc	gatggctaac	540
gtaccatagg	atggtatctc	tgttgtcgat	attggagcag	ccgtctctag	cattttcaat	600
tctccacagg	aatttttagg	caaggccgtg	gggctcaagt	cagaagcact	aaacaatcac	660
caatatgctg	atgtttttgc	caaggctttg	gggaaagaag	tcagagattg	aagaactcat	720
tgtgctatag	atgaccagaa	aacagttgaa	gaaggtttca	tggaagacgt	gggcttgagt	780
tggtccttga	gggaacaatga	ccatgtatag	acagagaggg	catcaagaag	gctggcctgtg	840
ctaatctctg	aataaacacg	acaaaccaga	ggcagtcagg	gaaggaggca	aattctggct	900
ctgcctctat	ccttgattac	ccgggaagct	ttcgagaagc	tgaggattcc	tcagacaaag	960
gaaatagcca	atatgtgtcg	tttctatgaa	atgaagccag	accgagatgt	caatctcacc	1020
caccaactaa	atcccaaatg	caaaagcttc	agccatttta	tctcagagaa	ccagggagcc	1080

```

ttcaaggcca tgtagaaat cagctgttca gataggcctc tgcaccacac agcctctttc 1140
ctctctgac ctcttctctc ttacggcaca acattcatgt tgacagaaca tgctgggaatg 1200
caattgtttg caacaccgaa ggatttctctg cgtgtgcctc ttcaagttaga agcaactgcot 1260
tggtgatagg acacggtaat ttgattcaca tttaacttgc tagttagtga taagggttgg 1320
acaactgttt ggtaaaaatga gaagcctcgg aacttggagc ttctctccta ccactaatgg 1380
gagggcagat tatactggga ttctctctcg gtgagtaatt tcaagcccta atgctgaaat 1440
tcctccaggc agctccagtt ttctcaactg cattgcaaaa ttcccagtga acttttaagt 1500
acttttaact taaaaaaatg aacatctttg tagagaattt tctggggaac atggtgttca 1560
atgaacaagc acaagcattg gaaatgctaa aattcagttt tgctcacaaga ttggaagtgt 1620
attttctgac tcaattcatga agtcatctat tgagccacca ttcaattatt catctattaa 1680
ttctctgac ctctcaattat ccattctgca aacttttctt gagcaccagc acgggtggoc 1740
attgtgtgac ttctctcatc tcctatgtgt ttctttatca aagtgtacca ctctgaaag 1800
gotctcttcc agtctgttgt tggttcaag tcattgccagg gccagggggc ccatctctc 1860
gtttagctct aggcaaaatc caggggatct gcagtgggga gcggggggcag gaagctggag 1920
ggaagggcctg tgaagggatg ggatgtggaa agacaagggt acagaaggac ccaataggac 1980
ctttctatat ctctggctta gcattttcta catcatattg taatcgtctt atttgcctagt 2040
ttctctcttc actgtgagtg actaacagtc atctttatcc cagtgccttg tacataataa 2100
gtgatcaata aatgttgatt gactaaatga aaaaaaaaaa aaaaaaaa 2148

```

<210> 155

<211> 153

<212> PRT

<213> Homo sapiens

<400> 155

```

Met Thr Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
1      5      10      15
Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
20     25     30
Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
35     40     45
Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
50     55     60
Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
65     70     75     80
Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
85     90     95
Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
100    105    110
Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
115    120    125
Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
130    135    140
Glu Asn Gln Gly Ala Phe Lys Gly Met
145    150

```

<210> 156

<211> 128

<212> PRT

<213> Homo sapiens

<400> 156

```

Met Thr Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
1      5      10      15
Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
20     25     30
Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly

```

35	40	45
Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys		
50	55	60
Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp		
65	70	75
Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Thr Ile		
85	90	95
Cys Ala Ile Asp Asp Gln Lys Thr Val Glu Glu Gly Phe Met Glu Asp		
100	105	110
Val Gly Leu Ser Trp Ser Leu Arg Glu His Asp His Val Ala Gly Ala		
115	120	125

<210> 157

<211> 424

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 320, 322

<223> n = A,T,C or G

<400> 157

```

ctgcagccg ggggagccac tagtccagtg tgggtggaatt cattggtctt tacaagactt 60
ggatacatta cagcagacat ggaatatataa ttttaaaaaa tttctctcca acctccttca 120
aattcagtc cactgtttat attacctttct ccaggaaccc tccagtgggg aaggctgcga 180
tattagattt ccttgatgac aaagtttttg ttgaaagctg tgctcagagg aggtgagagg 240
agaggaagga gaaaactgca tcataacttt acagaattga atctagagtc ttccccgaaa 300
agcccagaaa cttctctgcn gnatctggct tgtccatctg gtctaagggt gctgcttctt 360
ccccagccat cgagtcagtt tgtgcccatt aataatacac gacctgctat ttccccatgac 420
tgct

```

<210> 158

<211> 2099

<212> DNA

<213> Homo sapiens

<400> 158

```

ccgcgggttaa aaggcgagc aggtggggagc cggggccttc acccgaaacc cgacgagagc 60
ccgacagccg gcggcgcccg agcccgacct gcctgcccag ccgagagcgaa gggcgccgcc 120
ccgcgcagag ccgcgcgccg ggccgcgggc cgcagagcag ttaaaacgtg caggcaccag 180
aaggcaactc ctgtcggtga agaagacctg tctccggtgt cacgggcatc ctgtgttttg 240
caaacggggc tgacctccct tctctggggag cagggaaggtg cagggaagga aaagaagtaa 300
agaagatctg gctaaacaat ttctgtatgg cgaaagaaaa attotaactt ttacgacctc 360
ttcatgcatc tttaattcaa ttggaatatt ccaggcgaca tctctactga ccgagcaaa 420
attgacatcc gtatcatcac tgtgcacctt tggctttctag gcactccagt ggggtaggag 480
aaggaggctc gaaacctcgc cagagggatc ttgcctcat tctttgggtc tgaacctg 540
gcagtctgtg gaaacaggac tcagggataa accagcgcaa tggattgggg gacgctgcac 600
actttcatcg ggggtgtcaa caaacactcc accagcatcg ggaaggtgtg gatcacagtc 660
atctttatct tccgagtcac gatcctcgtg gtggctgccc aggaagtgtg ggggtgagag 720
caagaggact tctgtcgcaa cacactgcaa ccgggatgca aaaatgtgtg ctatgaccac 780
tttttccggc tgtccacat ccggtctgtg gccctccagc tgatcttcgt ctccacccca 840
gcgctgctgt tggccatgca tgtggcctac tacaggcagc aaacctctcg caagtccagg 900
cgaggagaga agaggaatga ttccaagac atagaggaca ttaaaaagca gaaggttcgg 960
atagagggtt cgctgtgggt gacgtacacc agcagcatct ttttcgaaat catctttgaa 1020
gcagccttta tgtatgtgtt ttaacttcct tacaatgggt accacctgcc ctgggtgttg 1080
aaatgtggga ttgacctcgc ccccaacctt gttgactgct ttatttctag gccaacagag 1140

```

```

aagaccgtgt ttaccatttt tatgattttt gcgtctgtga tttgcatgct gcttaacgtg 1200
gcagagtgtt gctacotgct gctgaaagtg tgttttagga gatcaaaagag agccacagacg 1260
caaaaaaatc accccaatca tgccctaaag gagagtaagc agaataaagt gaatgagctg 1320
atttcagata gtgtgtcaaaa tgcaatcaca ggttcccaag ctaaacattt caaggttaaaa 1380
tgtagctcgc tcataaggag acttctgtct tctccagaag gcaataccaa cctgaaagt 1440
cctctctgag cotgaagagt ttgtaaatga ctttcataat aaatagacac ttgagttaac 1500
ttttgttagg atacttgcct cattcataca caacgtaatc aaatatgtgg tccactctctg 1560
aaaaacaagag actgcttgac aaaggagcat tgcagtcact ttgacaggtt ccttttaagt 1620
ggactctctg acaagtgagg tactttctga aaatttatat aactgttgtt gataaggaac 1680
atttatccag gaattgatac gtttatttagg aaaagatatt ttataggctt tggagtgttt 1740
tagttctgac ttgtgaattta tataaagtat tttataatg actggtcttc cttacctgga 1800
aaaaacatgcc atgttagttt tagaattaca ccacaagtat ctaaaattgg aacttaacaa 1860
gggtctatct tgtaaatatt gttttgcatt gtctgttggc aaattttgga actgtcatga 1920
tacgtttaag gtggaaagtg ttcattgcac aatatattt tactgtcttc tgaatgtaga 1980
cggaacagtg tgggaagcaga aggccttttt aactcatcgc tttgccaatc attgcaaaaa 2040
actgaaatgt ggatgtgatt gcttcaataa agctcgtccc cattgcttaa aaaaaaaaaa 2099

```

```

<210> 159
<211> 291
<212> PRT
<213> Homo sapiens

```

```

<400> 159
Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
1      5      10      15
Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
20     25     30
Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
35     40     45
Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
50     55
Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
65     70     75     80
Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
85     90     95
Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
100    105    110
Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys Gln Lys Val Arg Ile
115    120    125
Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
130    135    140
Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
145    150    155    160
Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
165    170    175
Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
180    185    190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195    200    205
Glu Leu Cys Tyr Leu Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
210    215    220
Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
225    230    235    240
Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
245    250    255
Thr Gly Ser Gln Ala Lys His Phe Lys Val Lys Cys Ser Cys Val Ile
260    265    270
Arg Arg Leu Leu Ser Ser Pro Glu Gly Asn Thr Asn Leu Lys Val Pro

```

275
Ser Val Ala
290

280

285

<210> 160
<211> 3951
<212> DNA
<213> Homo sapiens

<400> 160

tctgcatcca	tattgaaaac	ctgacacaat	gtatgcagca	ggctcagtg	gagtgaactg	60
gaggcttcct	tacaacatga	cccaaaggag	cattgcagg	cctatttgca	acotgaagtt	120
tgtagctctc	ctgggtgcct	taagttcaga	actcccattc	ctgggagctg	gagtagacgt	180
tcaagacaat	gggtataatg	gattgtcat	tgcaattaat	cctcaggtag	ctgagaatca	240
gaacctcatc	tcaaacatta	aggaaatgat	aactgaagct	tcattttacc	tatttaatgc	300
taccaagaga	agagtatttt	tcagaaatat	aaagatttta	atacctgcca	catggaaagc	360
taataataac	agcaaaataa	aaCaagaatc	atatgaaaag	gcaaatgtca	tagtgactga	420
ctgggtatggg	gcacatggag	atgatccata	caccctacaa	tacagagggg	gtggaaaaga	480
gggaaaatac	attcatttca	cacctaat	cctactgaat	gataacttaa	cagctggcta	540
cggtacacga	ggccgagtg	ttgtccatga	atggggccac	ctccgttggg	gtgtgttcga	600
tgagtataac	aatgacaac	ctttctacat	aaatgggcaa	aatcaaat	aagtgacaag	660
gtgttctatct	gacatcacag	gcatttttgt	gtgtgaaaaa	ggctcctggc	cccaagaaaa	720
ctgtatttatt	agtaagcttt	ttaaagaagg	atgcaccttt	atctacaata	gcacccaaaa	780
tgcactgcga	tcaataatgt	tcattgcaag	tttatctctt	gtgggtgaat	tttgtaatgc	840
aagtaccacc	aaccaagaag	caccaaacct	acagaaccag	atgtgcagcc	tcagaagtgc	900
atgggtagta	atcacagact	ctgctgactt	tcaccacagc	tttcccatga	acgggactga	960
gcttccacct	ctcccacat	tctcgttgt	agaggctggt	gacaaaagg	tcgttttagt	1020
ctgggatgtg	tcagacaaga	tgccagaggg	tgacagactc	cttcaactac	aacaagccgc	1080
agaattttat	ttgatgcaga	tttgtgaaat	tcataccttc	gtgggcattg	ccagtttcga	1140
cagcaaaagc	gagatcagag	cccagctaca	ccaatttaac	agcaatgatg	atcgaaaagt	1200
gctggtttcca	tatctgccca	ccactgtatc	agctaaaaa	gacatcacga	tttgttccag	1260
gottaagaaa	ggattttgag	tggttgaaaa	actgaatgga	aaagcttatg	gctctgtgat	1320
gatatttagt	accagcggag	atgataagct	tcttggaact	tgcttaccga	ctgtgctcag	1380
cagtggttcca	acaattccat	ccattgccct	gggttccatc	gcagcccccga	atctggagga	1440
attatccagt	cttacaggag	gtttaaagtt	ctttgttcca	gatataacca	actccaatag	1500
catgattgat	gctttccagta	gaatttccct	tggaactgga	gacattttcc	agcaacatat	1560
tcagcttgaa	actgcagggt	aaaatgtcaa	acctcacctat	caattgaaaa	acacagtgac	1620
tggtgataat	actgtgggca	acgacactat	gtttctagtt	acgtggcagg	ccagtggtcc	1680
ctctgagatt	atatttatgt	atcctgatgg	acgaaaatac	tacacaaata	attttatcac	1740
caatctaact	tttcggacag	ctagtctttg	gattccaggga	acagctaaag	ctggggcactg	1800
gccttaaccc	taactaacat	cccacattc	tctgcaagcc	ctgaaagtga	cagtgacctc	1860
tcgcgcctcc	acctcagctg	tgcccaccag	cactgtggaa	gcctttgtgg	aaagagacag	1920
ctctccatttt	ctctcatcctg	tgatgattta	tgccaatgtg	aaacaggagat	tttatcccat	1980
tttcaatgcc	actgtcactg	ccacagtgta	gccagagact	ggagatccctg	ttacgctgag	2040
actccttgat	gatggagcag	gtgctgatgt	tataaaaaat	gatggaattt	actcagggta	2100
ttttttctcc	tttgtgcgaa	atggtagata	tagcttgaaa	gtgcattgca	atcactctcc	2160
cagcataaag	acccacagccc	actctattcc	aggagtgcat	gctatgtgta	taccaggtta	2220
cacagcaaac	ggctaatttc	agatgaatgc	tccaaggaaa	tcagtagtca	gaaatgagga	2280
ggagcgaaag	tggggcttta	gccaggtcag	ctcaggaggc	tccttttccg	tgctgggag	2340
tcocagctggc	ccccaccctg	atgtgtttcc	accatgcaaa	attattgacc	tggaagctgt	2400
aaaagttaga	ggagaattga	ccctatcttg	gcagcacctt	ggagaagact	ttgatccagg	2460
ccaggctaca	agctatgaaa	taagaatgag	taaaagtcta	cagaatatcc	aaagtacttt	2520
taacaatgct	attttagtaa	atatacaca	gcgaatatct	cagcaagctg	gcatacggga	2580
gatattttag	ttctccaccc	aaatttcac	gaatggacct	gaacatcagc	caaatggaga	2640
aacacatgaa	agccacagaa	tttatgttgc	ataacagcga	atggatagga	actccttaca	2700
gtctgctgta	tctaacattg	cccagggccc	tctgtttatt	ccccccaatt	ctgatcctgt	2760
acctgccaga	gattatctta	tattgaaagg	agttttaaca	gcaatggggt	tgataggaat	2820

```

catttgcctt attatagttg tgacacatca tactttaagc agggaaaaa gagcagacaa 2880
gaaagagaaat ggaacaaaat tattataaat aaatatccaa agtgtcttcc ttcttagata 2940
taagaccatc gcccttcgac tacaaaaaca tactaacaaa gtcaaatata catcaaaact 3000
gtattaaaat gcattagatt ttgttacaat acagataaga tttttacatg gtatagcaac 3060
aaattctttt tgggggtaga ttagaaaacc cttacacttt ggctatgaac aaataataaa 3120
aattattctt taaagtaatg tctttaaagg caaagggaag ggtaaaagtc gaccagtgtc 3180
aaggaaagtt tgttttaatt aggtggaaaa atagcccaa gcagagaaaa ggagggtagg 3240
tcctgattat aactgtctgt gtgaagcaat catttagtta ctttgattaa tttttctttt 3300
ctccttatct gtgcagaaca ggttgcttgt ttacaactga agatcatgct atattcata 3360
tatgaagccc ctaatgcaaa gctctttacc tcttgctatt ttgttatata tattacagat 3420
gaaatctcac tgcataatgc cagagatctt ttttactgt aagaggtaac ctttaacaat 3480
atgggtatta cctttgtctc ttcataccgg ttttatgaca aaggtctatt gaattatttt 3540
gtttgtaagt ttctactccc atcaaaagcag ctttttaagt tattgccttg gttattatgg 3600
atgatatgta tagcccttat aatgccttaa ctaagggaag aaagatgtta ttctgagttt 3660
gttttaatac atatatgaac atatatgttt attcaatata accaaaagaag aggtcagcag 3720
ggagatacta acccttggaa atgattagct ggctctgttt ttgtgttaaa taagagtctt 3780
taatcctttc tccatcaaga gttacttacc aagggcaggg gaagggggat atagaggtcc 3840
caaggaaaaa aaaatcatct ttcatcttta attttactcc ttccctctat ttttttaaaa 3900
gattatcgaa caataaaatc atttgccttt ttaattaaaa acataaaaaa a 3951

```

<210> 161

<211> 943

<212> PRT

<213> Homo sapiens

<400> 161

```

Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val
1 5 10 15
Thr Leu Leu Val Ala Leu Ser Ser Glu Leu Pro Phe Leu Gly Ala Gly
20 25 30
Val Gln Leu Gln Asp Asn Gly Tyr Asn Gly Leu Leu Ile Ala Ile Asn
35 40 45
Pro Gln Val Pro Glu Asn Gln Asn Leu Ile Ser Asn Ile Lys Glu Met
50 55 60
Ile Thr Glu Ala Ser Phe Thr Leu Phe Asn Ala Thr Lys Arg Arg Val
65 70 75 80
Phe Phe Arg Asn Ile Lys Ile Leu Ile Pro Ala Thr Trp Lys Ala Asn
85 90 95
Asn Asn Ser Lys Ile Lys Gln Glu Ser Tyr Glu Lys Ala Asn Val Ile
100 105 110
Val Thr Asp Trp Tyr Gly Ala His Gly Asp Asp Pro Tyr Thr Leu Gln
115 120 125
Tyr Arg Gly Cys Gly Lys Glu Gly Lys Tyr Ile His Phe Thr Pro Asn
130 135 140
Phe Leu Leu Asn Asp Asn Leu Thr Ala Gly Tyr Gly Ser Arg Gly Arg
145 150 155 160
Val Phe Val His Glu Trp Ala His Leu Arg Trp Gly Val Phe Asp Glu
165 170 175
Tyr Asn Asn Asp Lys Pro Phe Tyr Ile Asn Gly Gln Asn Gln Ile Lys
180 185 190
Val Thr Arg Cys Ser Ser Asp Ile Thr Gly Ile Phe Val Cys Glu Lys
195 200 205
Gly Pro Cys Pro Gln Glu Asn Cys Ile Ile Ser Lys Leu Phe Lys Glu
210 215 220
Gly Cys Thr Phe Ile Tyr Asn Ser Thr Gln Asn Ala Thr Ala Ser Ile
225 230 235 240
Met Phe Met Gln Ser Leu Ser Ser Val Val Glu Phe Cys Asn Ala Ser
245 250 255

```


Thr His Asn Gln Glu Ala Pro Asn Leu Gln Asn Gln Met Cys Ser Leu
 260 265 270
 Arg Ser Ala Trp Asp Val Ile Thr Asp Ser Ala Asp Phe His His Ser
 275 280 285
 Phe Pro Met Asn Gly Thr Glu Leu Pro Pro Pro Pro Thr Phe Ser Leu
 290 295 300
 Val Glu Ala Gly Asp Lys Val Val Cys Leu Val Leu Asp Val Ser Ser
 305 310 315 320
 Lys Met Ala Glu Ala Asp Arg Leu Leu Gln Leu Gln Ala Ala Glu
 325 330 335
 Phe Tyr Leu Met Gln Ile Val Glu Ile His Thr Phe Val Gly Ile Ala
 340 345 350
 Ser Phe Asp Ser Lys Gly Glu Ile Arg Ala Gln Leu His Gln Ile Asn
 355 360 365
 Ser Asn Asp Asp Arg Lys Leu Leu Val Ser Tyr Leu Pro Thr Thr Val
 370 375 380
 Ser Ala Lys Thr Asp Ile Ser Ile Cys Ser Gly Leu Lys Lys Gly Phe
 385 390 395 400
 Glu Val Val Glu Lys Leu Asn Gly Lys Ala Tyr Gly Ser Val Met Ile
 405 410 415
 Leu Val Thr Ser Gly Asp Asp Lys Leu Leu Gly Asn Cys Leu Pro Thr
 420 425 430
 Val Leu Ser Ser Gly Ser Thr Ile His Ser Ile Ala Leu Gly Ser Ser
 435 440 445
 Ala Ala Pro Asn Leu Glu Glu Leu Ser Arg Leu Thr Gly Gly Leu Lys
 450 455 460
 Phe Phe Val Pro Asp Ile Ser Asn Ser Asn Ser Met Ile Asp Ala Phe
 465 470 475 480
 Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln
 485 490 495
 Leu Glu Ser Thr Gly Glu Asn Val Lys Pro His His Gln Leu Lys Asn
 500 505 510
 Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe Leu Val
 515 520 525
 Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe Asp Pro Asp
 530 535 540
 Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn Leu Thr Phe Arg
 545 550 555 560
 Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys Pro Gly His Trp Thr
 565 570 575
 Tyr Thr Leu Asn Asn Thr His His Ser Leu Gln Ala Leu Lys Val Thr
 580 585 590
 Val Thr Ser Arg Ala Ser Asn Ser Ala Val Pro Pro Ala Thr Val Glu
 595 600 605
 Ala Phe Val Glu Arg Asp Ser Leu His Phe Pro His Pro Val Met Ile
 610 615 620
 Tyr Ala Asn Val Lys Gln Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val
 625 630 635 640
 Thr Ala Thr Val Glu Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu
 645 650 655
 Leu Asp Asp Gly Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr
 660 665 670
 Ser Arg Tyr Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys
 675 680 685
 Val His Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile
 690 695 700
 Pro Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn
 705 710 715 720

```

Ile Gln Met Asn Ala Pro Arg Lys Ser Val Gly Arg Asn Glu Glu Glu
      725      730      735
Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser Val
      740      745      750
Leu Gly Val Pro Ala Gly Pro His Pro Asp Val Phe Pro Pro Cys Lys
      755      760      765
Ile Ile Asp Leu Glu Ala Val Lys Val Glu Glu Glu Leu Thr Leu Ser
      770      775      780
Trp Thr Ala Pro Gly Glu Asp Phe Asp Gln Gly Gln Ala Thr Ser Tyr
      785      790      795      800
Glu Ile Arg Met Ser Lys Ser Leu Gln Asn Ile Gln Asp Asp Phe Asn
      805      810      815
Asn Ala Ile Leu Val Asn Thr Ser Lys Arg Asn Pro Gln Gln Ala Gly
      820      825      830
Ile Arg Glu Ile Phe Thr Phe Ser Pro Gln Ile Ser Thr Asn Gly Pro
      835      840      845
Glu His Gln Pro Asn Gly Glu Thr His Glu Ser His Arg Ile Tyr Val
      850      855      860
Ala Ile Arg Ala Met Asp Arg Asn Ser Leu Gln Ser Ala Val Ser Asn
      865      870      875      880
Ile Ala Gln Ala Pro Leu Phe Ile Pro Pro Asn Ser Asp Pro Val Pro
      885      890      895
Ala Arg Asp Tyr Leu Ile Leu Lys Gly Val Leu Thr Ala Met Gly Leu
      900      905      910
Ile Gly Ile Ile Cys Leu Ile Ile Val Val Thr His His Thr Leu Ser
      915      920      925
Arg Lys Lys Arg Ala Asp Lys Lys Glu Asn Gly Thr Lys Leu Leu
      930      935      940

```

<210> 162

<211> 498

<212> DNA

<213> Homo sapiens

<400> 162

```

tggagaacca cgtggacagc accatgaaca tgttggcgcg gggaggcagt gctggccgga 60
agccctctaa gtccgggtatg aaggagctgg ccgtgttcgc ggagaagctc actgagcagc 120
accggcagat gggcaagggt ggcaagcatc accttggcct ggaggagccc aagaagctgc 180
gaccaccccc tgccaggact cctgccaac aggaactgga ccaggtctcg gacggatctc 240
ccaccatgcg ccttcgggat gagcggggcc cctctggagca cctctactcc ctgcacatcc 300
ccaactgtga caagcatggc ctgtacaacc tcaaacagtg gcaagatgic tctgaacggg 360
cagcgtgggg agtgctgggt tgtgaacccc aacaccggga agctgatcca gggagccccc 420
accatccggg gggaccocga gtgtcatctc ttctacaatg agcagcagga ggctcgggg 480
gtgcacaccc cagcggat

```

<210> 163

<211> 1128

<212> DNA

<213> Homo sapiens

<400> 163

```

gccactggc cctcctgac gagcacac gcacttgaaa cttgttctca ggggtgtgtg 60
aatcaacttt ccggaagcaa ccagccacc agaggaggtc ccgagcgcg cgagagacga 120
tgacggcgag actggttcag cagtggagcg tcgcggtgtt cctgtctgagc tacgcggtgc 180
cctcctcgcg gcgctcggtg gaggtgtctca gcgcgcgcct caaaagagct gtgtctgaac 240
atcagctcct ccatgacaag ggaagtgcca tccaagatt acggcgacga ttcttccttc 300
accatctgat cgcagaatc cacacagctg aaatcagagc tacctggag gtgtccctca 360

```

```

actccaagcc ctctccaac acaagaagcc acccgctccg atttgggtct gatgatgagg 420
gcagataccct aactcagaa actaacaagg tggagacgta caaagagcag ccgctcaaga 480
cacctgggaaa gaaaaagaaa ggcaagcccg ggaacagcaa ggagcaggaa aagaaaaaac 540
ggcgaactcg ctctgcttgg ttagactctg gagtacttgg gattgggcta gaaggggacc 600
acctgtctga cacctccaca acgtgcttgg agctogattc acggaggcat tgaatatctt 660
agcagagacc ttccaaggac atattgcagg attctgtaat agtgaacata tggaaagtat 720
tagaataatt tatgtctgtt aaataactgt aatgcatttg aataaaactg tctcccccat 780
tgcctctatga aactgcacat tggctcattt gaataatttt ttttttgcaa aggctaatcc 840
aattattatt atcaacttta ccatatttta ttttgcctat ttagtatttt attttgtaaa 900
tgtatcttgg tgctgctgaa tttctatatt ttttgaaca taatgcactt tagatataca 960
tatcaagtat gtgtgataat gacacaatga agtgcctcta tttgtgtggt gattttaagt 1020
aatgcctaaa tataattatc caaattgatt ttcttctgtg catgtaaaaa taacagtatt 1080
ttaaatttgt aaagaattgt taataaataa taactaattt acatcatg 1128

```

<210> 164

<211> 1310

<212> DNA

<213> Homo sapiens

<400> 164

```

gggcctgtgtt cgcaagaag ctgacttcag agggggaaac tttctcttt taggaggcgg 60
ttagccctgtt tccacgaacc caggagaact gctggccaga ttaattagac attgctatgg 120
gagacgtgta aacacactac ttatcattga tgcataatata aaacattttt atttttgcga 180
ttatttcaga ggaagcgctt ctgatttgtt tcttttttcc ctttttgcct tttctgtgct 240
tgtgtgttgg agaaagcaca gttggagtag ccggttgcta aataagtccc gagcgcgagc 300
ggagacgatg cagcggagac tggttcagca gtggagcgct gcggtgttcc tgcgtgagta 360
cgcggtgccc tcttgcgggc gctcggtgga gggctctcag cgcgcgctca aaagagctgt 420
gtctgaacat cagctctccc atgacaaggg gaagtccatc caagatttat ggccgacgatt 480
cttctctcac catctgatcg cagaaatcca cacagctgaa atcagagcta ctcgagaggt 540
gtcccctaac tccaagccct ctcccaacac aaagaaccac cccgtccgat ttgggtctga 600
tgatgagggc agatacctaa ctacaggaac taacaaggtg gagacgtaca aagagcagcc 660
gtcacaagaca cctgggaaga aaagaagaag caagcccggg aaacgcaagg agcaggaaaa 720
gaaaaaacgg cgaaactgct ctgcctgtgtt agactctgga gtgactggga gtgggctaga 780
aggggaccac ctgtctgaca cctccacaac gtcgctggag ctgattcac ggagcgatg 840
aaattttcag cagagacctt ccaaggacat attgcaggat tctgtaaatg tgaacatatt 900
gaaagtatta gaaatattta ttgtctgtaa atactgtaaa tgcattggaa taaaactgtc 960
tccccattgt ctctatgaaa ctgcacattg gtcattgtga atattttttt ttttgcgaag 1020
gctaattccaa ttattattat cacatttacc ataatttttt ttgtccattg atgtatttat 1080
tttgtaaatg tatcttgggt ctgctgaatt tctatatttt ttgtaacata atgcacttta 1140
gatatacata tcaagtattg tgataaatga cacaatgaag tgcctctatt ttgtggttga 1200
ttttaatgaa tgcctaaaata taattatcca aattgatttt cctttgtgccc cgtaaaaata 1260
acagtatttt aaatttgtaa agaattgtcta ataaaatata atctaattac 1310

```

<210> 165

<211> 177

<212> PRT

<213> Homo sapiens

<400> 165

```

Met Gln Arg Arg Leu Val Gln Gln Trp Ser Val Ala Val Phe Leu Leu
1          5          10          15
Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
20          25          30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
35          40          45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
50          55          60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro

```

```

65          70          75          80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
      115
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145      150      155      160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
      165      170      175
His

```

```

<210> 166
<211> 177
<212> PRT
<213> Homo sapiens

```

```

<400> 166
Met Gln Arg Arg Leu Val Gln Gln Trp Ser Val Ala Val Phe Leu Leu
1      5      10      15
Ser Tyr Ala Val Pro Ser Cys Gly Arg Ser Val Glu Gly Leu Ser Arg
      20      25      30
Arg Leu Lys Arg Ala Val Ser Glu His Gln Leu Leu His Asp Lys Gly
      35      40      45
Lys Ser Ile Gln Asp Leu Arg Arg Arg Phe Phe Leu His His Leu Ile
      50      55      60
Ala Glu Ile His Thr Ala Glu Ile Arg Ala Thr Ser Glu Val Ser Pro
      65      70      75      80
Asn Ser Lys Pro Ser Pro Asn Thr Lys Asn His Pro Val Arg Phe Gly
      85      90      95
Ser Asp Asp Glu Gly Arg Tyr Leu Thr Gln Glu Thr Asn Lys Val Glu
      100      105      110
Thr Tyr Lys Glu Gln Pro Leu Lys Thr Pro Gly Lys Lys Lys Gly
      115      120      125
Lys Pro Gly Lys Arg Lys Glu Gln Glu Lys Lys Lys Arg Arg Thr Arg
      130      135      140
Ser Ala Trp Leu Asp Ser Gly Val Thr Gly Ser Gly Leu Glu Gly Asp
145      150      155      160
His Leu Ser Asp Thr Ser Thr Thr Ser Leu Glu Leu Asp Ser Arg Arg
      165      170      175
His

```

```

<210> 167
<211> 3362
<212> DNA
<213> Homo sapiens

```

```

<400> 167
cacaatgtat gcagcaggct cagtgtgagt gaactggagg cttotctaca acatgaccca 60
aaggagcatt gcaggctcta ttgcaacct gaagttgtg actotcctgg ttgccttaag 120
ttcagaactc ccattcctgg gagctggagt acagcttcaa gacaatgggtg ataattggatt 180

```

gctcattgca attaatcctc aggtacctga gaatcagaac ctcattctcaa acattaagga 240
 atagataact gaagcttcac ttacactatt taatgtctacc aagagaagag tatttttccag 300
 aaataataag attttaatac ctgccacatg gaaagctaata aataacagca aaataaaaaa 360
 agaatacatat gaagaaggcaa atgtcatagt gactgactgg tatggggcac atggagatga 420
 tccatacacc ctacaatata gagggtgtgg aaaagaggga aaatacattc atttcacacc 480
 taattttctca ctgaatgata acttaacagc tggctacgga tccagaggcc gagtgtttgt 540
 ccatgaatgg gccaccctcc gttgggggtg gttcgtagag tataacaagt acaaaccttt 600
 ctacataatg gggcaaaatc aaattaaagt gacaaggtgt tcatctgaca tccacagcat 660
 ttttgttgtt gaaaaaggtc cttgcccoca agaaaaactgt attattagta agctttttta 720
 agaaggatgc accctttatct acaatagcac ccaaaatgca actgcatcaa taatgttcat 780
 gcaaaagtta ttctctatgt ttgaattttg taatgcagat accocaacac aagaagcacc 840
 aaacctacag aaccagatgt gcagcctcag aagtgcattg gatgtaata cagactctgc 900
 tgactttcac cacagctttc ccatgaacgg gactgagctt ccactctctc ccaactotte 960
 gcttgtagag gctggtgaca aagtgtctgt tttagtctgt gatgtgtcca gcaagatggc 1020
 agaggctcat agactctctc aactacaaca agccgcagaa ttttatttga tgcagattgt 1080
 tgaattctac accctctgtg gcattgccag tttcgacagc aaaggagaga tcagagccca 1140
 gctacaccaa attaacagca atgatgatcg aaagtgtctg gtttcatatc tgcacccacc 1200
 tgtatcaagt aaaaacagca tcagcatttg ttcaagggtt aagaaggatg ttgaggttgt 1260
 tgaaaaactt aatggaaaag ctattggctc tgtgatgata ttagtgaaca gggagatga 1320
 taagttctct ggcaattgct tacccactgt gctcagcagt ggttcaacaa ttcactcttt 1380
 tgccctgggt tcatctgcag ccccaaatct ggaggaatta tcaactctta caggaggttt 1440
 aaagtctctt gttccagata tatcaaaact caatagcatg attgatgtct tcagtgaagt 1500
 ttctcttgga actggagaca ttttccagca acatatctag cttgaaagta caggtgaaaa 1560
 tgtcaaacct caccatcaat tgaaaaacac agtgactgtg gataatactg tgggcaacga 1620
 cactatgttt ctagttaact ggcaggccag tggctctctc gagattatat tattgtacc 1680
 tgaatggaga aaatactaca caaataattt tatcaccaat ctactcttct ggacagctag 1740
 tctttggatt ctagcctgg gcaactggact tacacactga tgtgtttcca 1800
 cactgcaaaa tttattgacct ggaagctgta aaagtagaag aggaattgac cctatcttgg 1860
 acagcacctg gagaagactt tgatcaggcc caggctacaa gctatgaat aagaatgagt 1920
 aaaaagtctac agaatactca agatgacttt aacaatgcta ttttagtaaa tacatcaag 1980
 cgaactctct cgaagctcgg catcaggagg atattttact tctcaaccca aatttccag 2040
 aatggacctg aacatcagcc aaatggagaa acacatgaaa gccacagaat ttatgttgca 2100
 atacgagcaa tggataggaa ctctttacag tctgctgtat ctactcttgc ccaggcgct 2160
 ctgtttatct cccccaattc tgatcctgta cctgccagag attatcttat attgaaagga 2220
 gtttttaacg caatgggttt gatggaatc atttgcotta ttatagtgtg gacacatcat 2280
 actttaagca gaaaaaagag agcagacaag atttgcaaat attataaata 2340
 aatatccaaa gtgtcttctc tcttagatat aagaccatg gccttgactt acaaaaacat 2400
 actcaaaaag tcaaatcaac atcaaaactg tattaaaatg cattgagttt ttgtacaata 2460
 cagataagat ttttcatggt tagatcaaca aattcttttt gggggtagat tagaaaaacc 2520
 ttactcttgt gctatgaaca aataataaaa attattcttt aaagtatactg ctttaaaggc 2580
 aaagggaggt gtaaagtctg accaggttca aggaaggttt gttttattga ggtggaaaaa 2640
 tagccccaag cagagaaaag gagggtaggt ctgcattata actgtctgtg tgaagcaate 2700
 atttagttac tttagtaaat tttcttttct tctttatctg tgcagaacag ttgtcttgtt 2760
 tacaactgaa gataotgcta tatttcatat atgaagcccc taatgcaaag ctcttttaact 2820
 cttgctattt tgttatatat attacagatg aaatctcact gctaatgctc agagatcttt 2880
 tttcactgta agaggttaacc tttacaacata tgggtattac ctttgcctct tcaacccgt 2940
 ttatgacaa aggtctattg attttatttg tttgtaagtt tctactccca tcaagcagc 3000
 ttcttaagtt attgctgttg ttattatgga tgaatgttat agcccttaac atgcttcaac 3060
 taaggagaag aagatgttat tctgagtttg ttttaataca tatatgaaca tatagtttta 3120
 ttcaattaaa ccaagaagaa ggtcagcagg gagatactaa cctttggaaa tgatttagct 3180
 gctgttgttt ttggttaaat aagagctctt aatcctttct ccactcaagag ttactacca 3240
 agggcgaggg aagggggata tagaggtcac aaggaaataa aaatcatctt tcatctttaa 3300
 ttttaactct tctcttattt tttttaaaaa attatcgaac aataaaatca tttgctcttt 3360
 tt 3362

<210> 168

<211> 2784

<212> DNA

<213> Homo sapiens

<400> 168

tctgcaccca	tattgaaaac	ctgacacaa	gtatgcagca	ggctcagtg	gagtgaactg	60
gaggcttctc	tacacatga	cccaaaggag	cattgcaggt	octatttgca	acctgaagtt	120
tgtgactctc	ctggttgcc	taagttcaga	actccattc	ctgggagctg	gagtagacgt	180
tcaagacaac	gggtataatg	gattgctcat	tgc aaat taat	octcaggtac	ctgagaatca	240
gaacctcatt	tcaacaatta	aggaaatgat	aactgaagct	tcattttacc	tattttaatgc	300
taccaagaga	agagtatttt	tcagaaatat	aaagatttta	atacctggcca	catggaaaagc	360
taataataac	agcaaaataa	aacaagaatc	atatgaaaag	gcaaatgtca	tagtgactga	420
ctgtgtatgg	gcacatggag	atgatccata	accctacaa	tacagaggtc	gtggaaaaga	480
gggaaataac	attcatttca	cacctaat	octactgaat	gataacttaa	cagctggccta	540
cggatcacga	ggcgagtggt	ttgtccatga	atgggcccac	ctccgttggg	gtgtgttcca	600
tgagtataac	aatgacaaac	ctttctacat	aaatgggcaa	aatcaaat	aagtgcacaa	660
gtgttcattc	gacatcacag	gcatttttgt	gtgtgaaaaa	ggctccttgc	cccaagaaaa	720
ctgtattatt	agtaagcttt	ttaaagaagg	atgcaccttt	atctacaata	gcacccaaaa	780
tgcactgcga	tcataaatgt	tcattgcgaag	tttattctct	gtggttgaat	tttgtaatgc	840
aaagtaccac	aaccaagaag	caccaaacct	acagaaaccg	atgtgcagct	tcagaagtgc	900
atgggatatg	atcacagact	ctctgcactt	tcaccaacgc	tttcccatga	acggggactga	960
gcttccacct	ctctccacat	tctcgttgtt	agaggtcgtg	gacaaagtgt	ctgtgtttagt	1020
gctggatgtg	tcacagaaga	tggcagaggc	tgacagactc	cttcaactac	aacaagccgc	1080
agaattttat	ttgatgcaga	ttgttgaat	tcatactctc	gtgggcattg	ccagtttcca	1140
gcacaaagga	gagatcacag	cccagctaca	ccaaat taac	agcaatgatg	atcgaaaagt	1200
gctggtttca	tatctgcccc	ccactgtatc	agctaaaaca	gacatcacga	tttgttccag	1260
gcttaagaaa	ggattttgag	tggttgaaaa	actgaatgga	aaagtcttat	gctctgtgat	1320
gatatttagt	accagcggag	atgataagct	tcttgccaat	tgcttaccoc	ctgtgctcag	1380
cagtggttca	acaattcaat	ccattgccct	gggttcaatc	gcagccccaa	atctggagga	1440
attatocagt	cttacaggag	gtttaaagtt	ctttgttcca	gataatatca	actccaatag	1500
catgtatgat	gctttcagta	gaatttctct	tggaaactgga	gacattttcc	agcaacatat	1560
tcagcttgaa	agtagcagtg	aaaatgtcaa	acctcaccat	caattgaaaa	acacagtgac	1620
tgtggataat	actgtgggca	acgacactat	gtttctagtt	acgtggcagg	ccagtggtcc	1680
tcctgagatt	atattatttg	atcctgatgg	acgaaaatac	tacacaaata	attttatcac	1740
caatctaact	tttccgacag	ctagtctttg	gattccaggga	acagctaagc	ctggggcactg	1800
gacttacacc	ctgaacaata	cccatcattc	tctgcgaagc	ctgaaagtga	cagtgacctc	1860
tgctgcctcc	aactcagctg	tgccccccagc	cactgtggaa	gcctttgtgg	aaagagacag	1920
ctccattttt	ctctactctg	tgatgattta	tgccaattgtg	aaacagggat	ttttatccat	1980
tottaatgct	actgtcactg	ccacagttga	gccagagact	ggagatcctg	ttacgctgag	2040
actccttgat	gtgggagcag	gtgctgatgt	tataaaaaat	gatggaaatt	actcgaggta	2100
ttttttctcc	tttctgcaa	atggtagata	tagcttgaaa	gtgcatgtca	atcacctccc	2160
cagcataagc	accccgagcc	actctatttc	agggagtcac	gctatgtatg	taccaggtta	2220
cacagcaaac	ggtaatatcc	agatgaatgc	tccagggaaa	ctagtaggca	gaatagagga	2280
ggagcgaaag	tggggcttta	gccgagtcag	ctcaggaggc	tccttttcag	tgctggggagt	2340
tcacgctgcy	ccccacccct	atgtgtttcc	accatgcmaa	attattgcac	tgggaagctgt	2400
aaatgaaga	ggaattgacc	ctatcttgga	cagcacctgg	agaagacttt	gatcagggcc	2460
aggtcacaga	ctatgaaata	agaatgagta	aaagtctaca	gaatatccaa	gatgacttta	2520
acaaatgcat	tttagtaaat	acatcaaaagc	gaaatctcca	gcaagctggc	atcagggaga	2580
tatttatggt	ctcaccccac	atttccacga	atggacctga	acatcagcca	aatggagaaa	2640
cacatgaaag	ccacagaatt	tatgttgcaa	tacgagcaat	ggataggaac	tccttacaagt	2700
ctgctgtatc	taacattgoc	caggcgctcc	tgtttattcc	ccccaatctc	gatcctgtac	2760
ctgcacagaga	tattcttata	ttga				2784

<210> 169

<211> 592

<212> PRT

<213> Homo sapiens

<400> 169

Met Thr Gln Arg Ser Ile Ala Gly Pro Ile Cys Asn Leu Lys Phe Val

1	5	10	15
Thr Leu Leu Val	Ala Leu Ser Ser	Glu Leu Pro Phe Leu Gly	Ala Gly
20		25	30
Val Gln Leu Gln	Asp Asn Gly Tyr	Asn Gly Leu Leu Ile	Ala Ile Asn
35		40	45
Pro Gln Val Pro	Glu Asn Gln Asn	Leu Ile Ser Asn	Ile Lys Glu Met
50		55	60
Ile Thr Glu Ala	Ser Phe Tyr Leu Phe	Asn Ala Thr Lys	Arg Arg Val
65		70	75
Phe Phe Arg Asn	Ile Lys Ile Leu Ile	Pro Ala Thr Trp	Lys Ala Asn
85		90	95
Asn Asn Ser Lys	Ile Lys Gln Glu Ser	Tyr Glu Lys Ala	Asn Val Ile
100		105	110
Val Thr Asp Trp	Tyr Gly Ala His	Gly Asp Asp Pro	Tyr Thr Leu Gln
115		120	125
Tyr Arg Gly Cys	Gly Lys Glu Gly	Lys Tyr Ile His	Phe Thr Pro Asn
130		135	140
Phe Leu Leu Asn	Asp Asn Leu Thr	Ala Gly Tyr Gly	Ser Arg Gly Arg
145		150	155
Val Phe Val His	Glu Trp Ala His	Leu Arg Trp Gly	Val Phe Asp Glu
165		170	175
Tyr Asn Asn Asp	Lys Pro Phe Tyr	Ile Asn Gly Gln	Asn Ile Lys
180		185	190
Val Thr Arg Cys	Ser Ser Asp Ile	Thr Gly Ile Phe	Val Cys Glu Lys
195		200	205
Gly Pro Cys Pro	Gln Glu Asn Cys	Ile Ile Ser Lys	Leu Phe Lys Glu
210		215	220
Gly Cys Thr Phe	Ile Tyr Asn Ser	Thr Gln Asn Ala	Thr Ala Ser Ile
225		230	235
Met Phe Met Gln	Ser Leu Ser Ser	Val Val Glu Phe	Cys Asn Ala Ser
245		250	255
Thr His Asn Gln	Glu Ala Pro Asn	Leu Gln Asn Gln	Met Cys Ser Leu
260		265	270
Arg Ser Ala Trp	Asp Val Ile Thr	Asp Ser Ala Asp	Phe His His Ser
275		280	285
Phe Pro Met Asn	Gly Thr Glu Leu	Pro Pro Pro Pro	Thr Phe Ser Leu
290		295	300
Val Glu Ala Gly	Asp Lys Val Val	Cys Leu Val Leu	Asp Val Ser Ser
305		310	315
Lys Met Ala Glu	Ala Asp Arg Leu	Leu Gln Leu Gln	Ala Ala Glu
325		330	335
Phe Tyr Leu Met	Gln Ile Val Glu	Ile His Thr Phe	Val Gly Ile Ala
340		345	350
Ser Phe Asp Ser	Lys Gly Glu Ile	Arg Ala Gln Leu	His Gln Ile Asn
355		360	365
Ser Asn Asp Asp	Arg Lys Leu Leu	Val Ser Tyr Leu	Pro Thr Thr Val
370		375	380
Ser Ala Lys Thr	Asp Ile Ser Ile	Cys Ser Gly Leu	Lys Lys Gly Phe
385		390	395
Glu Val Val Glu	Lys Leu Asn Gly	Lys Ala Tyr Gly	Ser Val Met Ile
405		410	415
Leu Val Thr Ser	Gly Asp Asp Lys	Leu Leu Gly Asn	Cys Leu Pro Thr
420		425	430
Val Leu Ser Ser	Gly Ser Thr Ile	His Ser Ile Ala	Leu Gly Ser Ser
435		440	445
Ala Ala Pro Asn	Leu Glu Glu Leu	Ser Arg Leu Thr	Gly Gly Leu Lys
450		455	460
Phe Phe Val Pro	Asp Ile Ser Asn	Ser Asn Ser Met	Ile Asp Ala Phe

465				470				475			480
Ser	Arg	Ile	Ser	Ser	Gly	Thr	Gly	Asp	Ile	Phe	Gln
				485				490			495
Leu	Glu	Ser	Thr	Gly	Glu	Asn	Val	Lys	Pro	His	His
			500					505			510
Thr	Val	Thr	Val	Asp	Asn	Thr	Val	Gly	Asn	Asp	Thr
			515				520				525
Thr	Trp	Gln	Ala	Ser	Gly	Pro	Pro	Glu	Ile	Ile	Leu
	530					535				540	545
Gly	Arg	Lys	Tyr	Tyr	Thr	Asn	Asn	Phe	Ile	Thr	Asn
	545				550			555			560
Thr	Ala	Ser	Leu	Trp	Ile	Pro	Gly	Thr	Ala	Lys	Pro
			565					570			575
Tyr	Thr	Leu	Met	Cys	Phe	His	His	Ala	Lys	Leu	Leu
		580						585			590

<210> 170

<211> 791

<212> PRT

<213> Homo sapiens

<400> 170

Met	Thr	Gln	Arg	Ser	Ile	Ala	Gly	Pro	Ile	Cys	Asn	Leu	Lys	Phe	Val
1				5					10					15	
Thr	Leu	Leu	Val	Ala	Leu	Ser	Ser	Glu	Leu	Pro	Phe	Leu	Gly	Ala	Gly
			20					25					30		
Val	Gln	Leu	Gln	Asp	Asn	Gly	Tyr	Asn	Gly	Leu	Leu	Ile	Ala	Ile	Asn
		35					40					45			
Pro	Gln	Val	Pro	Glu	Asn	Gln	Asn	Leu	Ile	Ser	Asn	Ile	Lys	Glu	Met
		50				55					60				
Ile	Thr	Glu	Ala	Ser	Phe	Tyr	Leu	Phe	Asn	Ala	Thr	Lys	Arg	Arg	Val
					70					75				80	
Phe	Phe	Arg	Asn	Ile	Lys	Ile	Leu	Ile	Pro	Ala	Thr	Trp	Lys	Ala	Asn
			85						90					95	
Asn	Asn	Ser	Lys	Ile	Lys	Gln	Glu	Ser	Tyr	Glu	Lys	Ala	Asn	Val	Ile
			100					105					110		
Val	Thr	Asp	Trp	Tyr	Gly	Ala	His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln
		115				120						125			
Tyr	Arg	Gly	Cys	Gly	Lys	Glu	Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn
	130				135						140				
Phe	Leu	Leu	Asn	Asp	Asn	Leu	Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg
	145				150				155					160	
Val	Phe	Val	His	Glu	Trp	Ala	His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu
			165					170						175	
Tyr	Asn	Asn	Asp	Lys	Pro	Phe	Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys
		180						185					190		
Val	Thr	Arg	Cys	Ser	Ser	Asp	Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys
		195						200				205			
Gly	Pro	Cys	Pro	Gln	Glu	Asn	Cys	Ile	Ile	Ser	Lys	Leu	Phe	Lys	Glu
	210					215					220				
Gly	Cys	Thr	Phe	Ile	Tyr	Asn	Ser	Thr	Gln	Asn	Ala	Thr	Ala	Ser	Ile
	225				230				235					240	
Met	Phe	Met	Gln	Ser	Leu	Ser	Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser
			245					250						255	
Thr	His	Asn	Gln	Glu	Ala	Pro	Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu
		260					265					270			
Arg	Ser	Ala	Trp	Asp	Val	Ile	Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser

		740						745						750	
Leu	Gly	Val	Pro	Ala	Gly	Pro	His	Pro	Asp	Val	Phe	Pro	Pro	Cys	Lys
		755					760					765			
Ile	Ile	Asp	Leu	Glu	Ala	Val	Asn	Arg	Arg	Gly	Ile	Asp	Pro	Ile	Leu
		770					775				780				
Asp	Ser	Thr	Trp	Arg	Arg	Leu									
785					790										

<210> 171

<211> 1491

<212> DNA

<213> Homo sapiens

<400> 171

```

cctcctgtcca gccaaagttaa gacatgctta cttcccccctt accttctcttc atgatgtgtgg 60
aagagtgtctg caaccacagc ctagcccaag ccgcatgaga gggagtgtgc cgagggtcttc 120
tgagaaggttt tctctcacat ctagaagaagaa gcgcttaaga tgtggcgagcc cctcttcttc 180
aagtgtgctct tgtcctgttg cctctgggagt tctcaaatgt ctgcagcagc cttccaccag 240
ctcgaggatg acatcaatac acagaggaag aagagtcagg aaaagatgag agaagtatac 300
gactctctctg ggcgaccocg agagcttacc attcctcaga cttcttcaca tgggtctaac 360
agatttgttc ctaaaagtaa agctctagag gccgtcaaat tggcaataga agccgggttc 420
caccatattg attctgcaca tgtttacaat aatgaggagc aggttggact ggccatccga 480
agcaagattg catagtgcag tgtgaagaga gaagacata tctacatttc aaagcttttg 540
agcaattccc atcgaccaga gttggtccga ccagccttgg aaaggtcact gaaaaatcct 600
caattggaact atgttgacct ctatcttatt cattttccag tgtctgtaaa gccaggtgag 660
gaagtgtatc caaaagatga aaatggaaaa atactatttg acacagtgtga tctctgtgcc 720
acatggggag ccatggagaa gtgtaaatgt gcaggatttg ccaagtccat cggggtgtcc 780
aactcaacc acaggctgct ggagatgac ctcaacaagc cagggtctcaa gtacaagcct 840
gtctgcaacc aggttgaatg tcatccttac ttcaaccaga gaaaactgct ggatttctgc 900
aagtcaaaag acattgttct ggttgccat agtgctctgg gatcccatg agaagaacca 960
tgggtggacc cgaactcccc ggtgctcttg gaggaccagc tctcttggtc cttggcaaaa 1020
aagcacaagc gaaccccagc cctgattgct ctgcgctacc agctgcagcg tggggtgtgt 1080
gtcctggcca agagctacaa tgagcagcgc atcagacaga acgtgcaggt gtttgaattc 1140
cagttgacct cagaggagat gaaagccata gatggcctaa acagaaatgt gcgatatttg 1200
acccttgata tttttgtctg ccccccataat tatccatttt ctgatgaata ttaacatgga 1260
gggcattgca tgaggtctgc cagaaggccc tgcgtgtgga tgggtgacac gaggatggct 1320
ctatgctgtg gactggacac atcgctctct gttaaattct tctgtcttgg cgacttcagt 1380
aagctacagc taagcccatc gcccggaaaa gaaagacaat aattttgttt ttcattttga 1440
aaaaattaaa tgctctctcc taaagattct tcacctaaaa aaaaaaaaaa a 1491

```

<210> 172

<211> 364

<212> PRT

<213> Homo sapiens

<400> 172

```

Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly
1 5 10 15
Ser Ser Gln Ile Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile
20 25 30
Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp
35 40 45
Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
50 55 60
Gly Ala Asn Arg Phe Val Pro Lys Ser Lys Ala Leu Glu Ala Val Lys
65 70 75 80
Leu Ala Ile Glu Ala Glu Phe His His Ile Asp Ser Ala His Val Tyr

```

			85				90				95			
Asn	Asn	Glu	Gln	Val	Gly	Leu	Ala	Ile	Arg	Ser	Lys	Ile	Ala	Asp
			100				105					110		
Gly	Ser	Val	Lys	Arg	Glu	Asp	Ile	Phe	Tyr	Thr	Ser	Lys	Leu	Trp
			115				120					125		
Asn	Ser	His	Arg	Pro	Glu	Leu	Val	Arg	Pro	Ala	Leu	Glu	Arg	Ser
			130				135				140			
Lys	Asn	Leu	Gln	Leu	Asp	Tyr	Val	Asp	Leu	Tyr	Leu	Ile	His	Phe
			145				150				155			160
Val	Ser	Val	Lys	Pro	Gly	Glu	Glu	Val	Ile	Pro	Lys	Asp	Glu	Asn
			165							170			175	
Lys	Ile	Leu	Phe	Asp	Thr	Val	Asp	Leu	Cys	Ala	Thr	Trp	Glu	Ala
			180						185				190	
Glu	Lys	Cys	Lys	Asp	Ala	Gly	Leu	Ala	Lys	Ser	Ile	Gly	Val	Ser
			195				200					205		
Phe	Asn	His	Arg	Leu	Leu	Glu	Met	Ile	Leu	Asn	Lys	Pro	Gly	Leu
			210				215				220			
Tyr	Lys	Pro	Val	Cys	Asn	Gln	Val	Glu	Cys	His	Pro	Tyr	Phe	Asn
			225				230				235			240
Arg	Lys	Leu	Leu	Asp	Phe	Cys	Lys	Ser	Lys	Asp	Ile	Val	Leu	Val
			245						250				255	
Tyr	Ser	Ala	Leu	Gly	Ser	His	Arg	Glu	Glu	Pro	Trp	Val	Asp	Pro
			260					265					270	
Ser	Pro	Val	Leu	Leu	Glu	Asp	Pro	Val	Leu	Cys	Ala	Leu	Ala	Lys
			275				280				285			
His	Lys	Arg	Thr	Pro	Ala	Leu	Ile	Ala	Leu	Arg	Tyr	Gln	Leu	Gln
			290				295				300			
Gly	Val	Val	Val	Leu	Ala	Lys	Ser	Tyr	Asn	Glu	Gln	Arg	Ile	Arg
			305				310			315			320	
Asn	Val	Gln	Val	Phe	Glu	Phe	Gln	Leu	Thr	Ser	Glu	Glu	Met	Lys
			325					330					335	
Ile	Asp	Gly	Leu	Asn	Arg	Asn	Val	Arg	Tyr	Leu	Thr	Leu	Asp	Ile
			340					345					350	
Ala	Gly	Pro	Pro	Asn	Tyr	Pro	Phe	Ser	Asp	Glu	Tyr			
			355				360							

<210> 173

<211> 1988

<212> DNA

<213> Homo sapiens

<400> 173

```

cgggagcgcg cccccgcgg cctcttcgct tttgtggcgg cgcccgcgct cgcaggccac 60
tctctgtgtg cgcccgctcc ggcgcgtcct ccgaccgcgt ccgctcggcc 120
ccgcgcgcgc cgtcaacatg atccgcgtcg gcttgccctg cgagcgctgc cgctggatcc 180
tgccccctgt cctactcagc gccatcgcc tgcacatcat ccgcgtggcc ggcccgggct 240
ggttgccagt tagcgaccac gccacagcgt cctcgtctgt gtggaatgc tcccaagagg 300
gcggcgccag cgggtcctac gaggaggcgt gtcagagcct catggagtac gggtggggtg 360
gagcagcgcc tgccatgctc ttctgtggtc tcatcatcct ggtgatctgt ttcattcctc 420
cctctcttgc cctctgtgga cccagatgc ttgtcttctc gagagtgatt ggaggtctcc 480
ttgccttggc tgctgtgttc cagatcatct ccttggtaat ttaccccggt aagtacaccc 540
agaccttacc ccttcatgcc aacctgcgtg tcacttacat ctataactgg gctacgggct 600
ttgggtgggc agccacgatt atcctgatcg gctgtgcctt cttcttctgc tgcctcccca 660
actacgaaga tgacctcttg ggcaatgccca agcccaggta cttctacaca tctgcctaac 720
ttgggaatga atgtggggaga aaatcgctgc tgctgagatg gactccagaa gaagaaactg 780
ttctccagc cgactttgaa cccatttttt ggcagtgctc atattattaa actagtcaaa 840
aatgctaaaa taatttggga gaaaattatt ttaagtagt gttatagttt catgtttatc 900

```

```

ttttattatg ttttgtgaag ttgtgtcttt tcactaatta cctatactat gccaatattt 960
ccttatatct atccataaca tttatactac atttgtgaaga gaatatgcac gtgaaactta 1020
acactttata aggtaaaaaat gaggtttcca agatttaata atctgatcaa gticttgtta 1080
tttccaaaata gaatggactt ggctgtttaa gggctaagga gaagaggaaag ataagggttaa 1140
aagttgttaa tgaccaaca tctctaaaaga aatgcacaaa aaaagtttat tttcaagcot 1200
tcgaactatt taaggaaagc aaaaatcatt cctaaatgca tatcatttgt gagaatctct 1260
cattaatact ctgaatcatt catttcagct aaggcttcac gttgaactga tatgtcatct 1320
aggaaagtac tatttcagtg tccaaacctg ttgccatagt ttgtaaggct ttcccttaag 1380
tgtgaaatat tttagatgaaa ttttctcttt taaagttctt tatagggtta ggggtgtgga 1440
aaatgctata ttaataaato tgtagtgttt tgtgtttata tgttcagacac cagagtagac 1500
tgagttgaaa gatggactgg gtctaattta tcatgactga tagatctgtg taagtgtgtg 1560
agtaaaagcat taggagggtc attcygttca caaaagtgcc actaaaacag cctcaggaga 1620
ataaatgact tgccttttcta aatctcaggt ttatctgggc tctatcatat agacaggctt 1680
ctgatagtgt gcarctgtaa gcagaaaact acatatagtt aaaatcctgg tctttctctg 1740
taaacagatt ttaaatgtct gatataaaac atgccacagg agaattcggg gatttgagtt 1800
tctctgaata gcatatata gatgcacagg ataggctatt atgatttttt accatttctga 1860
cttacataat gaaaaccaat tcatttttaa tatcagatta ttattttgta agttgtggaa 1920
aaagctaatt gtagttttca ttatgaagtt ttcccaataa accaggtatt ctaaaaaaa 1980
aaaaaaa

```

<210> 174

<211> 238

<212> PRT

<213> Homo sapiens

<400> 174

```

Gly Ala Ala Ser Pro Arg Pro Leu Arg Phe Cys Gly Gly Ala Arg Ala
1 5 10 15
Arg Arg Pro Leu Ser Ala Val Ala Arg Pro Ala Arg Ser Ser Asp Pro
20 25 30
Leu Arg Ser Ala Pro Leu Gly Pro Ala Pro Pro Val Asn Met Ile Arg
35 40 45
Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro Leu Leu Leu
50 55 60
Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly Arg Gly Trp
65 70 75 80
Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp Trp Lys Cys
85 90 95
Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly Cys Gln Ser
100 105 110
Leu Met Glu Tyr Ala Trp Gly Arg Ala Ala Ala Ala Met Leu Phe Cys
115 120 125
Gly Phe Ile Ile Leu Val Ile Cys Phe Ile Leu Ser Phe Phe Ala Leu
130 135 140
Cys Gly Pro Gln Met Leu Val Phe Leu Arg Val Ile Gly Gly Leu Leu
145 150 155 160
Ala Leu Ala Ala Val Phe Gln Ile Ile Ser Leu Val Ile Tyr Pro Val
165 170 175
Lys Tyr Thr Gln Thr Phe Thr Leu His Ala Asn Pro Ala Val Thr Tyr
180 185 190
Ile Tyr Asn Trp Ala Tyr Gly Phe Gly Trp Ala Ala Thr Ile Ile Leu
195 200 205
Ile Gly Cys Ala Phe Phe Phe Cys Cys Leu Pro Asn Tyr Glu Asp Asp
210 215 220
Leu Leu Gly Asn Ala Lys Pro Arg Tyr Phe Tyr Thr Ser Ala
225 230 235

```

<210> 175.
<211> 4181
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 3347, 3502, 3506, 3520, 3538, 3549, 3646, 3940, 3968, 3974,
4036, 4056, 4062, 4080, 4088, 4115
<223> n = A,T,C or G

<400> 175
ggtggatgcg tttgggttgt agctaggctt ttttttttot ttctctttta aaacacatct 60
agacaaggaa aaaaacaagcc toggatctga ttttttcaact ctcgttcttg tgcttggttc 120
ttactgtgtt tgtgtatttt aaaggcgaga agacaggggg aacaaaaacca gctggatcca 180
tccatccacg tgggtggttt taatttttctg ttttttctcg ttattttttt ttaaaaaaac 240
actcttcaca atgaacaaac tgtatatcgg aaacctcagc gagaacgcgc cccctcggga 300
cctagaagat actctcaagg acgccaagat cccggtgtcg ggacccttcc tgggtgaagac 360
tggtctacgcy ttctgttgact gcccgagcga gagctggggc ctcaaggcca tcgaggcgct 420
ttcagtgata atagaactga acgggaacc catagaagtt gagcaactcg tcccaaaaag 480
gcaaaagatt cggaaacttc agatacggaa tatcccgctt catttacctg gggaggtgct 540
ggatagttta ctagtccagt atggagtggg ggagagctgt gagcaagta gcaactgactc 600
ggaaactgca gttgtaaatg taacctatct cagtaaggag caagctagac aagcactaga 660
caaaactgaat ggaatttcagt tagagaattt caacttgaaa gtacgctata tccctgatga 720
aatggcgccg cagcaaaaacc ccttgcagca gcccgagggt cgccgggggc ttgggcagag 780
gggctctcca cggcaggggg ctccaggatc cgtatccaag cagaaaacct gtgatittgc 840
ttcggcgctg cttgttccca cccaatttgt tggagccatc ataggaagaag aaggtgcca 900
cattcggaac atcaccaaac agaccagctc taaaatcgat gtccaccgta aagaaaaatgc 960
ggggcgctgct gagaagtcga ttactatctt ctctactcct gaaggcactt ctgcggcttg 1020
taagatgat ctggagatta tgcataagga agctcaagat ataaaaatca cagaagagat 1080
ccoccttcta ttgtttagct ataataactt tgttggacgt ctatttgta aagaagaag 1140
aaatcttaaa aaaattgagc aagcacaga cactaaaaac acgatactc tcttcgagga 1200
attgacgctg tataatccag aacgcactat tacagttaaa ggcaatgttg agacatgtgc 1260
caaaagctgag gaggagatca tgaagaaat caggaggtct tatgaaaatg atattgcttc 1320
tatgaatctt caagcacatt taattctctg attaaatctg aacgccttgg gtctgttccc 1380
accocattca gggatgccac ctcccaacct tcagccatga cctctcccta 1440
cccgagtttt gagcaatcag aaacggagac tggttcatcg ttatcccag ctctatcagt 1500
cgggtgccatc atcgggaagc agggccagca catcaagcag ctttctcgtt ttgctggagc 1560
ttcaattaa gattgctcag cgggaagcacc agatgctaaa gtgaggatgg tgattatcac 1620
tggaaccacca gaggctcagt tcaaggctca gggagaat tttggaaaaa ttaagaaga 1680
aaaactttgt agtctaaag aagaggtgaa acttgaagct catatcagag tgccatctt 1740
tgctgctggc agagttattg gaaaaggagg caaaacgggt aatgaacttc agaatttgtc 1800
aagtgcagaa gtgtgtgtcc ctcgtgacca gacacctgat gagaatgacc aagtgtgtgt 1860
caaaataact ggtcacttct atgcttgcca ggttgccag agaaaaatc aggaaattct 1920
gactcagta aagcagcacc aacaacagaa agctctgcaa agtggaaccac ctcaagtaac 1980
acgggaagtaa agagctcaga aacagccac cacagaggca gatgccaaac caaagacaga 2040
ttgcttaacc aacagattgg cgctgaccoc ctatccagaa tccactgac aagtttttac 2100
ctagccagtt gtttctgagg accaggcaac ttttgaactc ctgtctctgt gagaatgat 2160
actttatgct ctctgaaatg tatgacacc agctttaaaa caaacaacaa aacaaaacaa 2220
aaaaggggtg gggaggagg gaaagagaag agctctgcac ttccctttgt tgtagtctca 2280
cagtataaca gatattctaa ttcttcttaa tattcccca taatgccaga aattgcttta 2340
atgatgcttt cactaaatc atcaaataga ttgctcctaa atccaattg taatatgtga 2400
tcagataat acttcaagga acttaaatgt taagccatta gcatagaaaa actgtctca 2460
gtttattttt tacctaacac taacatgagt aaactaagg aagtgtgata ttggttgagg 2520
aggggtattt aacgtgcatt tttactcaac taccctcaggt taatcagta acaatgaaa 2580
gcaaaatgtt tocttttttt tgaaaatttt atactatga ttatgataga agtccaacgc 2640
ttttttaaaa aataaatttt aaatttaaca gcaatcagct aacaggcaaa ttaagatttt 2700
tacttctggc tggtagacgt aaagctggaa aattaatttc aggggttttt gaggcttttg 2760

```

acacagttat tagttaaatc aaatgttcaa aaatcggag cagtgcctag tatctggaga 2820
gcagcactac catttatctt ttcatattata gttgggaaag tttttgacgg tactaacaaa 2880
gtggtgcacg gagatttttg aacggctgggt ttaaatggct tcaggagact tcagtttttt 2940
ttttagctac atgattgaat gcataataaa tgctttgtgc ttctgactat caatacctaa 3000
agaaagtgcg tcagtgaaga gatgcaagac ttccaactga ctggcaaaaa gcaagcttta 3060
gctttgtcta taggatgctt agttttgccac tacacttcaag accaatggga cagtcataga 3120
tggtgtgaca gtgtttaaac gcaacaaaag gctacatttc catggggcca gcactgtctat 3180
gagcctcact aagctatttt gaagattttt aagcactgat aaatataaaa aaaaaaaaaa 3240
aaattagact ccacctaag tagtaaaagta taacaggatt tctgtatact gtgcaatcag 3300
ttctttgaaa aaaaagtcac aagatagaga atacaagaaa agttttnggg atataatttg 3360
aatgactgtg aaaaacatgt accctttgata acgaaactcat ttgctcactc ctgcacagca 3420
aagcccagta cgtacaattg tgttgggtgt ggggtggtctc caaggccagc ctgctctctg 3480
aatgatgttt ttgagttttg gnttgaaga tgatcacagn catgtttacac tgatcttnaa 3540
ggacataatn tataacocct taacaaaaaa atccccctgcc tcattcttat ttcgagatga 3600
atttcgatac agactagatg tctttctgaa gatcaattag acattntgaa aatgatttaa 3660
agtgttttcc ttaagtttct ctgaaacaaa gtttcttttg tagttttaac caaaaagtg 3720
ccctttttgt cactggtttc tcttagcatt catgattttt ttttcacaca atgaattaaa 3780
attgctaaaa tcattgactg gctttctggg tggatttcaag gtaagatgtg ttttaaggcca 3840
gagcttttct cagtatttga ttttttccc caatatttga ttttttaaaa atatacacat 3900
aggagctgca ttttaaacct gctgggttaa attctgtcan atttcacttc tagcctttta 3960
gtatggcnaa tcanaattta cttttactta agcattttga attggagta tctggtacta 4020
gctaagaaat aactcnataa ttgagttttg tactcnocaa anatgggtca ttcctcatgn 4080
ataatgtncn cccaatgcag cttcatattc caganaacct gacgcaggat aaattttttc 4140
atcatttagt tccccaaaaa aaaaaaaaaa aaaaaaaaaa a 4181

```

<210> 176

<211> 579

<212> PRT

<213> Homo sapiens

<400> 176

```

Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
1 5 10 15
Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro
20 25 30
Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
35 40 45
Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
50 55 60
Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile
65 70 75 80
Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
85 90 95
Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln
100 105 110
Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser
115 120 125
Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
130 135 140
Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Met Ala Ala
145 150 155 160
Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln
165 170 175
Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
180 185 190
Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly
195 200 205
Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln

```

210	215	220
Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala		
225	230	235
Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala		240
	245	250
Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys		255
	260	265
Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val		270
	275	280
Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln		285
	290	295
Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu		300
305	310	315
Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys		320
	325	330
Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu		335
	340	345
Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu		350
	355	360
Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro		365
	370	375
Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Tyr Pro Gln Phe		380
385	390	395
Glu Gln Ser Glu Thr Glu Thr Val His Gln Phe Ile Pro Ala Leu Ser		400
	405	410
Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser		415
	420	425
Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp		430
	435	440
Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe		445
	450	455
Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val		460
465	470	475
Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser		480
	485	490
Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Lys Thr Val Asn Glu		495
	500	505
Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr		510
	515	520
Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr		525
	530	535
Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val		540
545	550	555
Lys Gln His Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser		560
	565	570
Arg Arg Lys		575

<210> 177

<211> 401

<212> DNA

<213> Homo sapiens

<400> 177

atgccccgta aatgtcttca gtgttcttca gggtagtgtg gatctcaaaa gatttggttc 60
 agatccaaac aaatacacat tctgtgtttt agtccagtgt tttctaaaaa aagaaactgc 120
 cacacagcaa aaaattgttt actttgttgg acaaaccaaa tcagttctca aaaaatgacc 180

```

ggtgcttata aaaagttata aatatcgagt agctctataaa caaacaccct gaccaagagg 240
gaagtgagct tgtgcttagt atttacattg gatgccagtt ttgtaatcac tgactttatgt 300
gcaaaactggt gcagaaattc tataaaactct ttgctgtttt tgataactgc tttttgttct 360
attttgtttt gttttgtaaa aatgataaaa cttcagaaaa t 401

```

<210> 178

<211> 561

<212> DNA

<213> Homo sapiens

<400> 178

```

acgcctttca aggggtgtacg caaagcactc attgataccc ttttggatgg ctatgaaaca 60
gcccgctatg ggacaggggt ctttggccag aatgagtacc tacgctatca ggaggccttg 120
agtgcactgg ccactgcggt taaagcagca attgggagct ctcagcgaca tcaccagtca 180
gcagccaaaag acctaaactca gtccctcgag gtctccccaa caaccatcca ggtgacatac 240
ctccctccca gtcagaagag taaacgtgcc aagcaacttc ttgaattgaa gagcttttaag 300
gataactata acacattgga gagtactctg tgacggagct gaaggacct tcgcgtatag 360
taagccagct agttgcaatg tgcaagacag gctgcttgcc gggccgcctct cggaacatct 420
ggcccgacag gcccgactg tatccatcca agttcccggt gtatccagag ttcttagagc 480
ttgtgtctaa agggtaattc cccaaccctt ccttatgagc atttttagaa cattggctaa 540
gactattttc cccagtagc g 561

```

<210> 179

<211> 521

<212> DNA

<213> Homo sapiens

<400> 179

```

cccaacgcgt ttgcataat tcccctggta gcctaacttc ttaccoccca atattggtaa 60
gatcgagcaa tggcttcagg acatgggttc tcttctctg tgatcattca agtgcctcat 120
gcataagacg tggcttgtct cagtgtttca acctcaccag ggctgtctct tggccacac 180
ctcgctccgt gttagtccg tatgacagcc cccatcaaat gaccttgccc aagtcaagg 240
ttctctgtgg tcaaggttgg ttggctgatt ggtggaaagt aggggtgacc aaaggaggcc 300
acgtgagcag tcagcaccag ttctgcacca gcagcgctc cgtcctagt ggtgttctg 360
ttctctctgg ccttgggtgg gctagggcct gattcgggaa gatgccttg cagggagggg 420
aggataagtg ggatctacca attgattctg gcaaaacaat ttctaagatt tttttgcttt 480
atgtgggaaa cagatctaaa tctcatttta tgcgtattt t 521

```

<210> 180

<211> 417

<212> DNA

<213> Homo sapiens

<400> 180

```

ggtggaattc gccgaagatg gcggagggtg aggtcctggt gcttgatggt cgaggccato 60
tctctggcgc cctggcgccc atcgtggcta aacaggctact gctggggcgg aaggtggtgg 120
tcgtacgcgt tgaaggcctc aacatttctg gcaatttcta cagaaaacaag ttgaagtacc 180
tggctttcct ccgcaagcgg atgaacacca accctcccg aggcctctac caattccggg 240
ccccagcgc catcttctgg cggaccgctg gaggtatgct gccccacaaa accaagcgag 300
gccaggcgcg ctgggacgtg ctcaagggtg ttgacggcat ccacccggcc tacgacaaga 360
aaaagcggat ggtggttctc gctgcctcca aggtcgtgag tctgaagcct acaagaa 417

```

<210> 181

<211> 283

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature
 <222> 35
 <223> n = A,T,C or G

<400> 181
 gattctcttct aaataggatg taaaacttct ttcnattac tcttccctag tctgtcctgc 60
 caagaactca agtgtaactg tgataaaaata acctttccca ggtaatttgg caggtatgtg 120
 tgaatactca gaatacacag gtgacataga tatgatatga caactggtaa tgggtggattc 180
 atttaccattg ttgactcttc tatgaccagg ccttaaggga aggtcagttt ttttaaaaaac 240
 caagtagtgt ctctctacct atctccagat acatgtcaaa aaa 283

<210> 182
 <211> 401
 <212> DNA
 <213> Homo sapiens

<400> 182
 atattcttgc tgcttatgca gctgacattg ttgcccctcc taaagcaacc aagtagcctt 60
 tatttccacc agtgaaagaa aacgctggcc tatcagttac attacaaaag gcagatttca 120
 agaggattga gtaagtagtt ggatggcttt cataaaaaca agaattcaag aagaggattc 180
 atgcttttaag aaacatttgt tatacattcc tcacaaatta tacctgggat aaaaactatg 240
 tagcaggcag tgtgtttttcc ttccatgtct ctctgcacta cctgcagttg gtccctctgag 300
 gctgcaagtc tgtctatct gaattcccag cagaagcact aagaagctcc accctatcac 360
 ctacagagata aaactatggg gaaaacttaa atctgtgcata a 401

<210> 183
 <211> 366
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 325
 <223> n = A,T,C or G

<400> 183
 acogtgtcca agtttttaga acccttggtt gccagacoga ggtgtcctgg tcaccgtttc 60
 accatcatgc tttgatgttc cctgtctttt ctctctctct ctctcaagag caaagggttaa 120
 ttttaaggaca aagatgaagt cactgtaaac taatctgtca ttgtttttac ctctcttttc 180
 tttttcagtg cagaaattaa aagtaagtat aaagcaccgt gattggggat gtttttgctg 240
 gtgtcggaat cactggtaaa tgttggctga gaacaatccc tccccttgca ctgtgtgaaa 300
 caacttgagc gctttaagag attancctga gaataatata aatatctttt ctcttcaaaa 360
 aaaaaa 366

<210> 184
 <211> 370
 <212> DNA
 <213> Homo sapiens

<400> 184
 tcttacttca aaagaaaaat aaacataaaa aataagttgc tggttcctaa caggaaaaat 60
 ttttaataatt gtaactgagag aaactgctta cgtacacatt gcagatcaaa tatttggagt 120
 taaaatgtta gtctacatag atgggtgatt gtaactttat tgccattaaa agatttcaaa 180
 ttgcatctcat gctctctgtg acacataaat aaaaaatggc gatctctcct 240
 tcagttctgct ctgttttaatt ctgctgtctg ctctctctca atgctgcgtc cctaattgta 300
 cacagtttag tgatatctag gagtataaag ttgtgcgccca tcaataaaaa tcacaaaagt 360
 ggttttaaaaa 370

```

<210> 185
<211> 107
<212> DNA
<213> Homo sapiens

<400> 185
ctcatattat tttccttttg agaaattgga aactctttct gttgctatta tattaataaa 60
gttggtgttt attttctggt agtcaccttc cccattttaa aaaaaaa 107

<210> 186
<211> 309
<212> DNA
<213> Homo sapiens

<400> 186
gaaaggatgg ctctggttgc cacagagctg ggacttcatg ttcttctaga gagggccaca 60
agagggccac aggggtggcc gggagttgtc agctgatgcc tgctgagagg caggaattgt 120
gcagtgtagt gacagtcattg agggagtgct tcttcttggg gaggaagaaa ggtagagcct 180
ttctgtctga atgaaaggcc aaggctacag tacaggggcc cgcgccagcc aggggtgttaa 240
tgcccaogta gtggaggcct ctggcagatc ctgcattcca aggtcactgg actgtacgtt 300
tttatggtt 309

<210> 187
<211> 477
<212> DNA
<213> Homo sapiens

<400> 187
ttcagtccta gcaagaagcg agaattctga gatcctccag aaagtcgagc agcaccacac 60
tccaaacctcg ggcagtgctc ttcaggcttt actggggacc tgcgagctgg cctaattgtg 120
tgccctgcaa gccaggccat cctggggcgc cacagacgag ctccgagcca ggtcaggott 180
cggaggccac aagctcagcc tcaggcccag gcactgattg tggcagaggg gccactaccc 240
aaggctctagc tagggccaag acctagttac ccagacagtg agaagccctt ggaaggcaga 300
aaagttggga gcatggcaga cagggaaggg aaacatttcc agggaaaaaa catgtatcac 360
atgtcttcag aagcaagtca ggtttcatgt aaccgagtgct cctcttgcgt gtccaaaagt 420
agcccagggc tgtgacacag gcttcacagt gattttgtgt tcagccgtga gtccacac 477

<210> 188
<211> 220
<212> DNA
<213> Homo sapiens

<400> 188
taaatatggt agatattaat attcctotta gatgaccagt gattccaatt gtcaccaagt 60
ttaaataagt accctgtgag tatgagataa attagtgaca atcagaacaa gtttcagtat 120
cagatgttca agaggaagtt gctattgcat tgaatttaat attgtacat aaacactgat 180
ttttttgagc attattttgt atttgttgta cttaataacc 220

<210> 189
<211> 417
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 76, 77
<223> n = A,T,C or G

```

```

<400> 189
accatcttga cagaggatcac atgctcccaa aacgtttgtt accacactta aaaactcactg 60
ccatcattaa gcatcnnttt caaaattata gccattcatg atttactttt tccagatgac 120
tatcatattt ctagtctcttt gaatttgtaa ggggaaaaaa aaaaacttacg 180
atgcactttt ctccagcaca tcagatttca aattgaaaaa taaagacatg ctatggtaat 240
gcacttgata gtaactacaca ctttgtacaa caaaaaacag aggcagaaga caacggaaag 300
agaaaagcct tcctttgttg gcccttaaac tgagtcaaga tctgaaatgt agagatgac 360
tctgacgata cctgtatgtt cttattgtgt aaataaaatt gctggtatga aatgaca 417

```

```

<210> 190
<211> 497
<212> DNA
<213> Homo sapiens

```

```

<400> 190
gcactggcgc gctctcccggt cccgcgggtg ttgctgtctg tgcgcgtgct gctgggcctg 60
aacgcaggag ctgtcattga ctggccacac gaggaggcca aggaagtatg ggattatgtg 120
acggctccga aggatgccta catgttctgg tggctctatt atgccacca cctcctgaag 180
aactctcag aactgccctt ggtcatgtgg cttcaggcgg gtcaggcggg ttctagcaact 240
ggatttgaa actttgagga aattgggccc cttgacagt atctcaaac acggaatacc 300
acctggctcc aggcgtccag tctctatatt gtggataatc ccgtgggcac tgggttcagt 360
tatgtgaatg gtatgggtgc ctatgccaa gacctggcta tgggtgcttc agacatgatg 420
gttctcctga agacctctt cagttgccac aaagaattcc agacagtcc attctacatt 480
ttctcagagt cctatgg 497

```

```

<210> 191
<211> 175
<212> DNA
<213> Homo sapiens

```

```

<400> 191
atgttgaata ttttgcttat taactttgtt tattgtcttc tccctcgatt agaataatag 60
ctacttgagt acaaggattt gagcctgtta cttactctgc tgaattttag gctcctggaa 120
gataccacgc attcaataga gaccacacaa taaatatatg tcaaataaaa aaaaa 175

```

```

<210> 192
<211> 526
<212> DNA
<213> Homo sapiens

```

```

<400> 192
agtaaacatt attatttttt ttatatttgc aaaggaaaca tatctaactc ttcctataga 60
aagaacagta ttgctgtaat tcttttctt ttcttctca tttcctctgc ccttataaag 120
attgaagaaa gagaaacttg tcaactcata tccacgttat ctagcaaaat acataagaat 180
ctatcaccaa gtaatgtatc cttcagaatg tgttggttta ccagtgcac ccataattca 240
tcacaaaatt aaagcaagaa gtccatagta atttatttgc taatagtgga tttttaatgc 300
tcagagtttc tgagggtcaaa ttttatcttt tcaactacaa gctctatgat cttaataat 360
ttacttaatg tatttttggtg tattttcttc aaattaatat tgggtgtcaa gactatattc 420
aatctctctg atcactttga gaacaaaact tttattaaat gtaaggcact tttctatgaa 480
ttttaaatat aaaaataaat attgttctga ttattactga aaaaaa 526

```

```

<210> 193
<211> 553
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature

```

<222> 290, 300, 411, 441

<223> n = A,T,C or G

<400> 193

tccattgtgg	tggaattcgc	tctctggtaa	aggcgtgcag	gtgttgcccg	cgccctctga	60
gctgggatga	gccgtgctcc	cgggtggaagc	aaggagagccc	agccggagccc	atggccagta	120
cagtggtgagc	agttggactg	accattgctg	ctgcaggatt	tgccaggccgt	tacgtttttgc	180
aagccatgaa	gcattatggag	cctcaagtaa	aacaagtttt	tcaaaagccta	ccaaaatctg	240
ccttcagtg	tggtatttat	agaggtgggt	ttgaacccaa	aatgacaaan	cggtgaagcan	300
cattaaact	aggtgtaagc	cctactgccca	ataaaggaa	aataagagat	gctcatcgac	360
gaattatgct	tttaaactcat	cctgacaaaag	gaggatctcc	ttatatagca	nccaaaatca	420
atgaagctaa	agattttacta	naaggtcaag	ctaaaaaatg	aagtaaatgt	atgatgaatt	480
ttaaagttcgt	attagtttat	gtatatgagt	actaagtttt	tataataaaa	tgccctcagag	540
ctacaaatttt	aaa					553

<210> 194

<211> 320

<212> DNA

<213> Homo sapiens

<400> 194

cccttcccaa	tccatcagta	aagaccccat	ctgccttgto	catgcogttt	cccaacaggg	60
atgtcaactg	atatgagaat	ctcaaatctc	aatgccttat	aagcatttct	tcctgtgtcc	120
attaagactc	tgataattgt	ctcccctcca	taggaatttc	tcccaggaaa	gaaatatato	180
cccactctcc	tttcatatca	gaactaccgt	cccgcgatatt	cccttcagag	agattaaaga	240
ccagaaaaaa	gtgagcctct	tcactctgcac	ctgtaaatagt	ttcagttcct	attttcttcc	300
attgaccocat	attttatacct					320

<210> 195

<211> 320

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 203, 218

<223> n = A,T,C or G

<400> 195

aagcatgacc	tggtgaaatg	gtcagacctt	gtatttgttt	tttggccttg	aaagtagcaa	60
gtgaccagaa	tctgccatgg	caacaggctt	taaaaaagac	ccttaaaaaa	acactgtctc	120
aaotgtggtg	ttagcaccag	ccagctctct	gtacatttgc	tagctgttag	ttttctaaaga	180
ctgagtaaac	ttcttatttt	tanaaagggg	aggctggntt	gtaactttcc	ttgtacttaa	240
ttgggtaaaa	gtcttttcca	caaaaccacca	tctattttgt	gaactttgtt	agtcattctt	300
tatttggtaa	attatgaact					320

<210> 196

<211> 357

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 36

<223> n = A,T,C or G

<400> 196

atataaaata	atacgaaaact	ttaaaaagca	ttggantgtc	agtatgttga	atcagtagtt	60
------------	-------------	------------	------------	------------	------------	----

```

tcactttaac  tgtaacaacat  ttcttaggac  accatttggg  ctagtttctg  tgtaagtgtg  120
aatactacaa  aaactttattt  atactgttct  tatgtcattt  gttatatcca  tagattttata  180
tgatgatgatg  acatctgtgct  aaaaagaaat  tattgcaaaa  ctaaccacta  tgtactttttt  240
tataaaact  gttatggacaa  aaaatggcat  tttttatatt  aaattgttta  gctctggcaa  300
aaaaaaaaa  ttttaagagc  tgggtactaat  aaaggattat  tatgactgtt  aaaaaaa  357

```

```

<210> 197
<211> 565
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 27
<223> n = A,T,C or G

```

```

<400> 197
tcagctgagt  accatcagga  tatttanccc  ttttaagtct  gttttgggag  tagaaaaacta  60
aagcaacaa  acttcctctt  gacagctttg  attggaatgg  ggttattaga  tcattcacct  120
tggctcctaca  cttttcttaga  tgcttgggtga  acataacacc  acttataatg  aacatccctg  180
gttcctatat  tttgggctat  gtgggttagga  attgttactt  gttactcgag  cagcagccct  240
agaaagttaag  ccaggggctt  cagatctaag  ttagtccaaa  agctaaatga  tttaaagtca  300
agttgtaatg  ctaggcataa  gcaactctata  atacattaaa  ttataggccg  agcaattagg  360
gaatgtttct  gaaacattaa  acttgtattt  atgtcactaa  aattctaaca  caaacttaaa  420
aaatgtgtct  catacatatg  ctgtactagg  cttcatcatg  cattttctaaa  tttgtgtatg  480
atttgaatat  atgaagaagt  ttatacaaga  gtgttattta  aaattattaa  aaataaatgt  540
ataataattg  tacctattgt  aaaaaa  565

```

```

<210> 198
<211> 484
<212> DNA
<213> Homo sapiens

```

```

<400> 198
tatgtaagta  ttggtgtctg  ctttaaaaaa  ggagaccag  acttcacctg  tccttttttaa  60
acatttgaga  acagtgttac  tctgagcagt  tgggccacct  tcaccttacc  cgacagctga  120
ctgttgggatg  tgtccattgt  cgcaggtttg  gctgttgccc  ggacaggaca  ggacctccat  180
tggggcgagc  agcaggtggc  aggggtgtgg  cttgaggtgg  gtggcagcgt  cttgttctcc  240
ttctgtgtgc  ttcttgagag  ggtctctaaa  gcagagtgtg  gttggccctg  ggggaagcag  300
agcagctatt  tctccctct  agtacctctg  catttggtag  tgttccctct  ggctttctga  360
agggcgagcag  actcttgagt  atactgcaga  ggacatgctt  tatcagtagg  tcctgagggc  420
tccaggggct  caactgacca  agtaacacag  aagttggggt  atgtggccta  tttgggtcgg  480
aaac  484

```

```

<210> 199
<211> 429
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 77, 88, 134, 151, 189, 227, 274, 319
<223> n = A,T,C or G

```

```

<400> 199
gcttatgttt  tttgttttaa  cttttgtttt  ttaacattta  gaattattaca  ttttgtatta  60
tacagtacct  ttctcanaca  ttttgtanaa  ttcatattcg  cagctcacta  ggattttgtg  120
gaacattaaa  aagngtgata  gcgatattag  ngccaatcaa  atggaaaaaa  ggtagtctta  180

```

```

ataaacaana cacaacgttt ttatacaaca tactttaaaa tattaanaaa actcettaat 240
attgttttct attaagtatt attctttggg caanattttc tgatgctttt gattttctct 300
caatttagca ttgtcttng gttttttct ctatttagca ttctgttaag gcacaaaaac 360
tatgtactgt atgggaaatg ttgtaaatat taccttttcc acatttttaa cagacaactt 420
tgaatccaa 429

```

<210> 200

<211> 279

<212> DNA

<213> Homo sapiens

<400> 200

```

gcttttttga ggaattacag ggaagctcct ggaattgtac atggatatct ttatccctag 60
ggggaaatca aggagctggg cacccttaatt tctttatgga agtggtttaa actattttta 120
ttttattaca agtattacta gagtagtggt tctactctaa gatttcaaaa gtgcatttaa 180
aatcatatat gttccgcctt gcaaatatat tgttattttg gtggagaaaa aaatagtata 240
ttctacataa aaaattaaag atattaacta agaaaaaa 279

```

<210> 201

<211> 569

<212> DNA

<213> Homo sapiens

<400> 201

```

taggtcagta tttttagaaa ctcttaatat ctcatactct tgataccaaa agcagccctg 60
attgtttaag cacacacctg cacaagaagc agtgatggtt gcattttacat ttctgtgggt 120
cacaaaaaaa aattctcaaa aagcaaggac ttacgctttt tgcaaaagcct ttgagaagtt 180
actggatcat aggaagctta taacaagaat ggaagattct taaataactc actttctttg 240
gtatccagta acagttagatg ttcaaaatat gtactgtatt aataccagca ttgtgaacgc 300
tgtcaaacct tgtgggtatt actaaagcaag ttactactag ctctgtaaaa gtacttctat 360
aattaatggt atttatacac tgccctccat gacttttaact ttgccctaag ctaattctca 420
aaactgtaaa tgctactcca atatcagaaa aaaaggggga ggtggaatta tatttctcgt 480
gattttaaga gtacagagaa tcatgcacat ctctgattag ttcatatatg tctagtgtgt 540
aataaaagtc aaagatgaac tctcaaaaa 569

```

<210> 202

<211> 501

<212> DNA

<213> Homo sapiens

<400> 202

```

attaataggc ttaataattg ttggcaagga tctttttgct ttctttggca tgcaagctcc 60
tagcatctgg cagtggggcc aagaaaaataa ggtttatgca tgtatgatgg tttttctctt 120
gagcaacatg attgagaacc agtgatgttc aacaggtgca ttgagatata ctttaaatga 180
tgtactctgt tggctctaac tggaactctgg tcaccttcca tccatgcaac aactgtttca 240
aatctttgac aatgaaatga agctcaatgt gcatatggat tcaatccacc accatcgatc 300
atagcaccac ctatcagcac tgaaaactct ttgtcattaa gggatcattg caagagcagc 360
gtgactgaca ttatgaagcc ctgtactgaa gacagcaagc tgttagtaca gaccagatgc 420
ttctttggca ggctcgttgt acctcttga aaacctcaat gcaagatagt gtttcagtgc 480
tggcatattt tgggaattctg c 501

```

<210> 203

<211> 261

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 36, 96

<223> n = A,T,C or G

<400> 203

gacaagctcc	tggtcttgag	atgtcttctc	gttaangaga	tgggcctttt	ggaggtaaag	60
gataaaatga	atgagttctg	tcatgattca	ctatnttata	acttgcatga	ccctttactgt	120
gttagctctt	tgaatgttct	tgaatattta	gacttctttt	gtaaacaaat	gatatgtcct	180
tatcattgta	taaaagctgt	tatgtgcaac	agtggtggaga	ttcctgtgtc	gattttaataa	240
aatacttaaa	cactgaaaaa	a				261

<210> 204

<211> 421

<212> DNA

<213> Homo sapiens

<400> 204

agcatctttt	ctacaacgtt	aaaattgcag	aagtagctta	tcattaaaaa	acaacaacaa	60
caacaataac	aataaatctc	aagtgtaaat	cagttattct	accccttacc	aaggatatca	120
gcctgttttt	tcctcttttt	ctcctgggaa	taattgtggg	cttcttccca	aatttctaca	180
gcctcttttc	tcttctcatg	cttgagcttc	cctgtttgca	cgcatgcgtg	tgccaggactg	240
gcttgtgtgc	ttggactcgg	ctccaggtgg	aagcatgctt	tccttggtta	ctgttggaga	300
aaactcaaac	ttcaagccct	aggtgtagcc	attttgtcaa	gtcatcaaat	gtatttttgt	360
actggcatta	acaaaaaaag	aagataaaat	atgttaccat	taaaacttta	taaaacttta	420
a						421

<210> 205

<211> 460

<212> DNA

<213> Homo sapiens

<400> 205

tactctcaca	atgaaggacc	tggaatgaaa	aatctgtgtc	taaacaagtc	ctctttagat	60
tttagtgcaa	atccagagcc	agcgtcggtt	gcctcgagta	attotttcat	gggtacottt	120
ggaaaagctc	tcaggagacc	tcacctagat	gcctattcaa	gctttggaca	gccactagat	180
tgtagcgcaa	gagcctttta	tttgaaagct	cattcttccc	cagacttgga	ctctgggtga	240
gaggaagatg	ggaaagaaga	gacagatttt	caggaagaaa	atcacatttg	tacottttaa	300
cagacttttg	aaaactacag	gactccaaat	tttcagtcct	atgacttgga	cacatagact	360
gaatgagacc	aaaggaaaag	cttaacatac	tacctcaagg	tgaaacttta	tttaaaagag	420
agagaatctt	atgtttttta	aatggagtta	tgaattttta			460

<210> 206

<211> 481

<212> DNA

<213> Homo sapiens

<400> 206

tgtggtggaa	ttcgggagcc	ccccagacc	tgacttttct	ctgcgtgggc	cgtctcctcc	60
tgcggaagca	gtgacctctg	accctcggtg	accttgcctt	tgagtgcctt	ttgaacgctg	120
gtcccgcggg	acttggtttt	ctcaagctct	gtctgtccaa	agacgctccg	gtcgaggtcc	180
cgctgcctct	gggtggatac	ttgaacccca	gacgcccctc	tgtgtcgtgt	tgctcggagg	240
cggtcttccc	atctgcctgc	ccaccgggag	ctctttccgc	cggtcgcagg	tcocagccc	300
acctcccgc	ctcagctcct	cggtgtgcgt	ctgggcaact	ctgcacaca	caatgcaagt	360
cctggcctcc	gcgcgcgc	gcccaacgga	gcgttaccgc	ccgccaactc	tgttatttat	420
ggtgtgacc	cctggagggtg	ccctcgcccc	accggggcta	tttattgttt	aattttattt	480
t						481

<210> 207

<211> 605

<221> misc_feature
 <222> 20, 21, 61
 <223> n = A,T,C or G

```
<400> 210
cgcccttgggg agccggcggn ngagtccggg acgtggagac ccggggtccc ggcagccggg 60
nggccgcggg gccacgggtg gggatgcacc gccgcggggg gggagctggc gccatcccaa 120
agaagaacct tgcagaggcc aagtataagg agcgagggac ggtcttggtt gaggaccagc 180
tagcccaagat gtcaaaagcag ttggacatgt tcaagaccaa cctggaggaa ttgtccagca 240
aacacaagca ggagatccgg aagaatcctg agttccgtgt gcagttccag gacatgtgtg 300
caaccattgg cgtggatccg ctggcctctg gaaaaggatt ttggtctcag atgctggggc 360
tgggggaact ctattacgaa ctaggtgtcc aaattatcga agtgtgcctg gcgctgaagc 420
atcggaatgg aggtctgata actttggagg aactacatca acaggtgttg aagggaaggg 480
gcaagttcgc ccaggatgtc agtcaagatg acctgatcag agccatcaag aaa 533
```

<210> 211
 <211> 451
 <212> DNA
 <213> Homo sapiens

```
<400> 211
ttagcttgag ccgagaacga ggcgagaaag ctggagaccg aggagaccgc ctagagcgga 60
gtgaacgggg aggggacgtg ggggacgggc ttgatcgtgc gcggacacct gctaccaagc 120
ggagcttcag caaggaaagt gaggagcgga gtgagaaacg gccctccagg cctgaggggc 180
tgcccaaggc agctagcctc acggaggatc gggacgctgg gcgggatgac gtgaagcgag 240
aagctgcctc accccacagt agcccctcga aggcggtctc ctctgaggag gagttagaga 300
agaaatccaa ggcgtatcatt gaggaatata tccatctcaa tgacatgaaa gaggcagtcc 360
agtgcgtgca ggagctggcc tcaacctcct tgctcttcac ctttgtacgg catggtgtcg 420
agctctacgt ggagcgcagt gccattgtc g 451
```

<210> 212
 <211> 471
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 54
 <223> n = A,T,C or G

```
<400> 212
gtgattatct ttgatcaggg agaagatcat ttagatttgt tttgcattcc ttanaatgga 60
gggcaacatt ccacagctgc cctggctgtg atgagtgtcc ttgcaggggc cggagtagga 120
gcactggggg gggggcgga ttggggttac tcgatgtaag ggattccttg ttgttgtgtt 180
gagatccagt gcagttgtga tttctgtgga tcccagcttg gttccaggaa ttttgtgtga 240
ttggcttaaa tcagattttc aatcttcgac agctgggctg gaacgtgaac tcagtagctg 300
aacctgtctg acccggtcac gttcttggtat cctcagaact ctttgccttt gtccgggttg 360
gggtgggaac tcacgtgggg agcgggtggc gagaaaatgt aaggattctg gaatacatat 420
tcaatgggac tttctctccc tctcctgctt cctcttttcc tgcctccaa c 471
```

<210> 213
 <211> 511
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 27, 63, 337, 442

<212> DNA

<213> Homo sapiens

<400> 207

```

acccctttttg gattcagggc tcttcacaat taaatgagt gtaatgaaac aaggtgaaaa 60
tatagaagca tccctttgta tactgttttg ctacttacag tgtacttggc attgctttat 120
ctcactggat tctcacggta ggattttctga gatcttaato taagctccaa agttgtctac 180
ttttttgatc ctagggtgct ccttttgttt tacagagcag ggtcacttga ttgtctagct 240
ggtggcagaa ttggcaccat tacccaggtc tgactgacca ccagtcagag gcactttatt 300
tgtatcatga aatgatttga aatcatttga aagcagcgaa gtctgataat gaatgccagc 360
tttctgtgtg ctttgaatac aaagactcca aatattctgg agaacctgga taaaagtttg 420
aagggctaga ttgggatttg aagacaaaat tgtaggaat cttacatttt tgcataaaca 480
aacattaatg aaagcaaaac attataaaag taattttaat tcaccacata cttatcaatt 540
tcttgatgct tccaaatgac atctaccaga tatggttttg tggacatctt tttctgttta 600
cataa                                     605

```

<210> 208

<211> 655

<212> DNA

<213> Homo sapiens

<400> 208

```

ggcgttgttc tggattcccg tcgtaactta aagggaaact ttcacaatgt ccggagccct 60
tgatgtcctg caaatgaagg aggaggatgt ccttaagttc cttgcagcag gaaccacctt 120
agggtggcacc aatcttgact tccagatgga acagtcacat tataaaagga aaagtgtatg 180
catctatatac ataaatctca agaggacctg ggagaagctt ctgctggcag ctgctgcaat 240
tgttgccatt gaaaaccctg ctgatgtcag tgttatatcc tccaggaata ctggccagag 300
ggctgtgctg aagtttgtcg ctgccactgg agccactcca attgctggcc gcttcaactc 360
tgggaaccttc actaaccaga tccaggcagc cttccgggag ccacggcttc ttgtggttac 420
tgacccacagg gctgaccacc agcctctcac ggaggcatct tatgttaacc tacctaccat 480
tgcgctgtgtg aacacagatt ctccctctcg ctatgtggac attgccatcc catgcaacaa 540
caagggagct cactcagttg gtttgatgtg gtggatgctg gctcgggaag ttctgcgcat 600
gcgtggcacc atttcccggtg aacacccatg ggaggtcatg cctgatctgt acttc 655

```

<210> 209

<211> 621

<212> DNA

<213> Homo sapiens

<400> 209

```

catttagaac atggttatca tccaagacta ctctaccctg caacattgaa ctcccaagag 60
caaatccaca ttctctttga gttctgcagc ttctgtgtaa atagggcagc tgtcgtctat 120
gcogtagaat cacatgatct gaggaccatt catggaagct gctaaaatag ctagtctggg 180
gagtccttcca taaggttttg catggagcaa acaaacagga ttaaacatagg ttgggttctc 240
tcagccctctc aaaagcatag ggccttagcct gcaggcttcc ttgggctttc ctgtgtgtgt 300
tagtttttga aacactatag catctgttaa gatccagtgt ccatggaaac cttccacatc 360
gcogtgactc tggactatat cagtttttgg tccctctgct gctaaacagc 420
ccagctggac cagtctgaat gtcttttctt tacacctatg tttttaataa gtcaaacctc 480
aagaaacaaat ctaaaccaag ttctgttgca tatgtgtttg tgaactctgt ttgttattta 540
gtaggctctc atattgcaat taacttgttt ttgtaactcc tgattctctc ttttcggata 600
ctattgatga ataagaatat t                                     621

```

<210> 210

<211> 533

<212> DNA

<213> Homo sapiens

<220>

<223> n = A,T,C or G

```
<400> 213
ctaattagaa  acttgctgta  cttttntttt  tcttttaggg  gtcaaggacc  ctctttatag  60
cincacattg  cctacaataa  attattgcag  cagtttgcaa  tactaaaata  ttttttatag  120
actttatatg  tttccttttg  ataaagggat  gctgcatagt  agagttgggt  taattaaact  180
atctcagcgg  ttccctcgct  ttccctctcg  ctccatagtc  ctcaattgtc  ttccaggggag  240
ctcttttaac  cttaaaagttc  tacatttcat  gctcttagtc  aaattctgtt  acccttttaa  300
taactcttc  cactgcatac  ttccatcttg  aattggnggt  tctaaattct  gaaactgtag  360
ttgagataca  gctatttaac  atttctggga  gatgtgcac  cctctctctt  gtgggtggcc  420
aagggttggt  tgcgttaact  anaactcctg  atatgcttca  gagaatttag  gcaaacactg  480
gccatggcgg  tgggagtact  gggagtaaaa  t
511
```

<210> 214

<211> 521

<212> DNA

<213> Homo sapiens

```
<400> 214
agcattgcga  aataatccct  aattttccac  taataatata  atgaaatgat  gttaagcttt  60
ttgaaaagtt  taggttaaac  ctactgttgt  tagattaagt  tatttgttgc  ttccctttat  120
ctggaatttg  gcattagctt  ttttatttta  accctcttta  attcttatcc  aattccatga  180
cttaagggtg  gagagctaaa  cactgggatt  ttgggataac  agactgacag  ttttgctaaa  240
ttataatcgg  cattgtacat  agaaaggata  tggctacctt  ttgttaaatc  tgcactttct  300
aaatacctaa  aaagggaagt  gaagtataaa  tcaatttttg  tataatctgt  ttgaacatg  360
agttttatgt  gcttaatat  agggctttgc  cctctttctg  taagtctctt  gggatctctg  420
gtagaagctg  ttctcattaa  acaccaaca  gttaagtcca  ttctctggta  ctgactacaa  480
attcgggttc  atattctact  taacaattta  aataaactga  a
521
```

<210> 215

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 17, 20, 60, 61, 365

<223> n = A,T,C or G

```
<400> 215
gagcggagag  cggaccngtn  agagccctga  gcagccccc  cgcgcgcgc  ggcctagttn  60
ncatcacacc  ccggggaggag  ccgcagctgc  cgcagccg  cccagtcacc  atcacccgaa  120
ccatgacagc  cgaggccgag  acccagcagc  cgcccgccg  ccccccgcgc  gcccccgcgc  180
tcagcgcgc  cgacaccaag  cccggcacta  cgggcagcgc  cgcagggagc  ggtggcccg  240
gcgccctcac  atcgcgcgcg  cctgcgcgcg  gggacaagaa  ggctcatgca  acgaagggtt  300
tgggaaacgt  aaaatggttc  aatgtaagga  acggaatag  ttctcatcac  aggaatgaca  360
ccaangaaga  tgtatttgt  c
381
```

<210> 216

<211> 425

<212> DNA

<213> Homo sapiens

```
<400> 216
ttactaacta  ggtcattcaa  ggaagtcaag  ttaacttaaa  catgtcacct  aaatgcactt  60
gatggtgttg  aaatgtccac  cttcttaaat  ttttaagatg  aactatgttc  taaagaagat  120
aacaggccaa  tctggaaggt  actccctgtt  tgctcagaa  tgtcagatat  ttggatgtt  180
gcataagagt  cctatttgcc  ccagttaatt  caacttttgt  ctgcctgttt  tgtggaetgg  240
```

```

ctggctctgt tagaactctg tccaaaaagt gcattggaata taacttgtaa agctccacc 300
aattgacaat atattgcat gtgtttaaac caaatccaga agcttaaac aatgagctg 360
cataatagta ttatttaaag aatcacaact gtaaacatga gaataactta aggatcttag 420
tttag 425

```

<210> 217

<211> 181

<212> DNA

<213> Homo sapiens

<400> 217

```

gagaaaccaa atgatagggt gtagagcctg atgactcoaa acaagccat caccgcgatt 60
cttcctcctt ctctcgtgct tacagctcca agggcccttc accttcattgt ctgaaatgga 120
actttggctt tticagtgga agaatagtgt gaaggtttca tttgttcta gaaaaaaaaa 180
a 181

```

<210> 218

<211> 405

<212> DNA

<213> Homo sapiens

<400> 218

```

caggccttcc agttcactga caaacatggg gaagtgtgcc cagctggctg gaaacctggc 60
agtgatacca tcaagcctga tgtccaaaag agcaagaat atttcccaa gcagaagtga 120
ggcctgggct gtattagtgc caggctgcgg tgggcagcca tgagaacaaa acctctctgt 180
tatttttttt ttccattagt aaaacacaag acttcagatt cagccgaatt gtggtgtctt 240
acaaggcagg ccttctctac aggggggtgga gagaccagcc ttctctcctt tggtaggaat 300
ggcctgagtt ggcgttgttg gcaggctact ggttgttatg atgtattagt agagcaacc 360
attaactttt tgtagtgttg attaaacttg aactgagaaa aaaaa 405

```

<210> 219

<211> 216

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 207, 210

<223> n = A, T, C or G

<400> 219

```

actccaagag ttagggcagc agagtggagc gatttagaaa gaacatttta aaacaatcag 60
ttaatttacc atgtaaaatt gctgtaaatg ataattgtga cagattttct gtcaaatat 120
tcaattgtaa acctctgttt aagactgtta cgtttctatt gcttttgtat gggatattgc 180
aaaaataaaa aggaaagaac cctcttnaan aaaaaa 216

```

<210> 220

<211> 380

<212> DNA

<213> Homo sapiens

<400> 220

```

cttacaaaatt gccccatgt gtaggggaca cagaaccott tgagaaaaact tagatttttg 60
tcgtatacaa gctcttgcc ttttcctct tcatttttt ccagtaacatt aaatttgta 120
atttcattct ttagggaaac tgatttagat ggttgtgttt gtgttctgat ggagaaaaa 180
gcaccccaag gactcagaag atgattttaa cagttcagaa cagatgtgtg caatattggt 240
gcattgtaata atgttgagt gcagtcacaaa gtcatgtatt ttatcttagt tcttcattac 300
tgcattgaaa aggaaacct gtctgagaaa atgcctgaca gttaatttta aaactatggt 360

```

gtaagtcctt gacaaaaaaa 380

<210> 221

<211> 398

<212> DNA

<213> Homo sapiens

<400> 221

```

ggttagtaag ctgtcgactt tgtaaaaaag ttaaaaaatga aaaaaaaagg aaaaatgaat 60
tgtatattta atgaatgaac atgtacaatt tgccactggg aggaggttcc tttttgttgg 120
gtgagtcctgc aagtgaattt cactgatgtt gatattcatt gtgtgtagtt ttatttcggg 180
cccagccccc tttcctttta ttttgagctt aatgccagct gcgtgtctag ttttgagtgc 240
agtataaatg aatcagcaaa tcaactctat ttttcacctc ttcccggtat tttttgggtt 300
gtttctgtgg gagcagtgta caccacactc tctgtatat tgcccttttg ctggaaaatg 360
ttgtatgttg aataaaattt tctataaaaa ttaaaaaa 398

```

<210> 222

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 49, 64

<223> n = A,T,C or G

<400> 222

```

ttcgataatt gatctcatgg gctttccctg gaggaagggt ttttttgnat gtttattttt 60
taanaacttg aaacttgtaa actgagatgt ctgtagcttt ttgcccac tcgtagtgtat 120
gtgaagattt caaaacctga gagcaacttt tctttgttta gaattatgag aaaggcacta 180
gatgacttta ggatttgcac ttttcccttt attgocctat ttcttgtgac gccgtgttgg 240
ggagggaat ctgtttattt ttctctacaa ataaaaagct aagattctat atcgcaaaaa 300
a 301

```

<210> 223

<211> 200

<212> DNA

<213> Homo sapiens

<400> 223

```

gtaagtgcct aggaagaaac ttgcaaaaa tttaatgagg atacactggt catttttaaa 60
attccttcac actgtaattt aatgtgtttt atattctttt gtagtaaaac aacataactc 120
agattttcac aggagacagt gggttttatt ggattgtcct ctgtaatagg ttccaataaa 180
gctggatgaa ctttaaaaaa 200

```

<210> 224

<211> 385

<212> DNA

<213> Homo sapiens

<400> 224

```

gaaaggtttg atccggactc aaagaaagca aaggagtgtg agccgccatc tgctggagca 60
gctgtaactg caagacctgg acaagagatt cgtcagcgaa ctgcagctca aagaacctt 120
tctccaaacac cagcaagccc taaccagggc cctcctccac aagtccagt atctcctgga 180
ccaccaaaag acagtcttgc ccttggttga cccccagaaa ggactgttac tccagcccta 240
tcataaatg ttgtaccaag acatcttggc tccctcgcta cttcagtcgc tgggaatgggt 300
aaacagagca cttaagtgtt tttcacagtt atattgtttt ctctggttac caataaaacg 360
ggccattttc aggtggtaaa aaaaa 385

```

<210> 225
 <211> 560
 <212> PRT
 <213> Homo sapiens

<400> 225

```

Met Glu Cys Leu Tyr Phe Leu Gly Phe Leu Leu Leu Ala Ala Arg
 1          5          10          15
Leu Pro Leu Asp Ala Ala Lys Arg Phe His Asp Val Leu Gly Asn Glu
 20          25          30
Arg Pro Ser Ala Tyr Met Arg Glu His Asn Gln Leu Asn Gly Trp Ser
 35          40          45
Ser Asp Glu Asn Asp Trp Asn Glu Lys Leu Tyr Pro Val Trp Lys Arg
 50          55          60
Gly Asp Met Arg Trp Lys Asn Ser Trp Lys Gly Gly Arg Val Gln Ala
 65          70          75          80
Val Leu Thr Ser Asp Ser Pro Ala Leu Val Gly Ser Asn Ile Thr Phe
 85          90          95
Ala Val Asn Leu Ile Phe Pro Arg Cys Gln Lys Glu Asp Ala Asn Gly
100          105          110
Asn Ile Val Tyr Glu Lys Asn Cys Arg Asn Glu Ala Gly Leu Ser Ala
115          120          125
Asp Pro Tyr Val Tyr Asn Trp Thr Ala Trp Ser Glu Asp Ser Asp Gly
130          135          140
Glu Asn Gly Thr Gly Gln Ser His His Asn Val Phe Pro Asp Gly Lys
145          150          155          160
Pro Phe Pro His His Pro Gly Trp Arg Arg Trp Asn Phe Ile Tyr Val
165          170          175
Phe His Thr Leu Gly Gln Tyr Phe Gln Lys Leu Gly Arg Cys Ser Val
180          185          190
Arg Val Ser Val Asn Thr Ala Asn Val Thr Leu Gly Pro Gln Leu Met
195          200          205
Glu Val Thr Val Tyr Arg Arg His Gly Arg Ala Tyr Val Pro Ile Ala
210          215          220
Gln Val Lys Asp Val Tyr Val Val Thr Asp Gln Ile Pro Val Phe Val
225          230          235          240
Thr Met Phe Gln Lys Asn Asp Arg Asn Ser Ser Asp Glu Thr Phe Leu
245          250          255
Lys Asp Leu Pro Ile Met Phe Asp Val Leu Ile His Asp Pro Ser His
260          265          270
Phe Leu Asn Tyr Ser Thr Ile Asn Tyr Lys Trp Ser Phe Gly Asp Asn
275          280          285
Thr Gly Leu Phe Val Ser Thr Asn His Thr Val Asn His Thr Tyr Val
290          295          300
Leu Asn Gly Thr Phe Ser Leu Asn Leu Thr Val Lys Ala Ala Ala Pro
305          310          315          320
Gly Pro Cys Pro Pro Pro Pro Pro Pro Arg Pro Ser Lys Pro Thr
325          330          335
Pro Ser Leu Gly Pro Ala Gly Asp Asn Pro Leu Glu Leu Ser Arg Ile
340          345          350
Pro Asp Glu Asn Cys Gln Ile Asn Arg Tyr Gly His Phe Gln Ala Thr
355          360          365
Ile Thr Ile Val Glu Gly Ile Leu Glu Val Asn Ile Ile Gln Met Thr
370          375          380
Asp Val Leu Met Pro Val Pro Trp Pro Glu Ser Ser Leu Ile Asp Phe
385          390          395          400
Val Val Thr Cys Gln Gly Ser Ile Pro Thr Glu Val Cys Thr Ile Ile
  
```

```

          405          410          415
Ser Asp Pro Thr Cys Glu Ile Thr Gln Asn Thr Val Cys Ser Pro Val
          420          425          430
Asp Val Asp Glu Met Cys Leu Leu Thr Val Arg Arg Thr Phe Asn Gly
          435          440          445
Ser Gly Thr Tyr Cys Val Asn Leu Thr Leu Gly Asp Asp Thr Ser Leu
          450          455          460
Ala Leu Thr Ser Thr Leu Ile Ser Val Pro Asp Arg Asp Pro Ala Ser
          465          470          475
Pro Leu Arg Met Ala Asn Ser Ala Leu Ile Ser Val Gly Cys Leu Ala
          485          490          495
Ile Phe Val Thr Val Ile Ser Leu Leu Val Tyr Lys Lys His Lys Glu
          500          505          510
Tyr Asn Pro Ile Glu Asn Ser Pro Gly Asn Val Val Arg Ser Lys Gly
          515          520          525
Leu Ser Val Phe Leu Asn Arg Ala Lys Ala Val Phe Phe Pro Gly Asn
          530          535          540
Gln Glu Lys Asp Pro Leu Leu Lys Asn Gln Glu Phe Lys Gly Val Ser
          545          550          555          560

```

<210> 226
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 226
 Ile Leu Ile Pro Ala Thr Trp Lys Ala
 1 5

<210> 227
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 227
 Phe Leu Leu Asn Asp Asn Leu Thr Ala
 1 5

<210> 228
 <211> 9
 <212> PRT
 <213> Homo sapiens

<400> 228
 Leu Leu Gly Asn Cys Leu Pro Thr Val
 1 5

<210> 229
 <211> 10
 <212> PRT
 <213> Homo sapiens

<400> 229
 Lys Leu Leu Gly Asn Cys Leu Pro Thr Val

```

1              5              10

<210> 230
<211> 10
<212> PRT
<213> Homo sapiens

<400> 230
Arg Leu Thr Gly Gly Leu Lys Phe Phe Val
1              5              10

<210> 231
<211> 9
<212> PRT
<213> Homo sapiens

<400> 231
Ser Leu Gln Ala Leu Lys Val Thr Val
1              5

<210> 232
<211> 20
<212> PRT
<213> Homo sapiens

<400> 232
Ala Gly Ala Asp Val Ile Lys Asn Asp Gly Ile Tyr Ser Arg Tyr Phe
1              5              10              15
Phe Ser Phe Ala
20

<210> 233
<211> 21
<212> PRT
<213> Homo sapiens

<400> 233
Phe Phe Ser Phe Ala Ala Asn Gly Arg Tyr Ser Leu Lys Val His Val
1              5              10              15
Asn His Ser Pro Ser
20

<210> 234
<211> 20
<212> PRT
<213> Homo sapiens

<400> 234
Phe Leu Val Thr Trp Gln Ala Ser Gly Pro Pro Glu Ile Ile Leu Phe
1              5              10              15
Asp Pro Asp Gly
20

```

<210> 235
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 235
 Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro
 1 5 10 15
 Pro Asn Ser Asp
 20

<210> 236
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 236
 Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr Ser Lys Arg
 1 5 10 15
 Asn Pro Gln Gln
 20

<210> 237
 <211> 21
 <212> PRT
 <213> Homo sapiens

<400> 237
 Arg Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu
 1 5 10 15
 Phe Ile Pro Pro Asn
 20

<210> 238
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 238
 Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg
 1 5 10 15
 Asn Ser Leu Gln
 20

<210> 239
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 239
 Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe Ser Pro
 1 5 10 15
 Gln Ile Ser Thr

20

<210> 240

<211> 21

<212> PRT

<213> Homo sapiens

<400> 240

Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser Leu Gln Asn
1 5 10 15
Ile Gln Asp Asp Phe
20

<210> 241

<211> 20

<212> PRT

<213> Homo sapiens

<400> 241

Glu Arg Lys Trp Gly Phe Ser Arg Val Ser Ser Gly Gly Ser Phe Ser
1 5 10 15
Val Leu Gly Val
20

<210> 242

<211> 20

<212> PRT

<213> Homo sapiens

<400> 242

Gly Ser His Ala Met Tyr Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile
1 5 10 15
Gln Met Asn Ala
20

<210> 243

<211> 20

<212> PRT

<213> Homo sapiens

<400> 243

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly
1 5 10 15
Ser His Ala Met
20

<210> 244

<211> 20

<212> PRT

<213> Homo sapiens

<400> 244

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu

1 5 10 15
 His Phe Pro His
 20

<210> 245
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 245
 Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu
 1 5 10 15
 Gln Ala Leu Lys
 20

<210> 246
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 246
 Asn Leu Thr Phe Arg Thr Ala Ser Leu Trp Ile Pro Gly Thr Ala Lys
 1 5 10 15
 Pro Gly His Trp
 20

<210> 247
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 247
 Leu His Phe Pro His Pro Val Met Ile Tyr Ala Asn Val Lys Gln Gly
 1 5 10 15
 Phe Tyr Pro Ile
 20

<210> 248
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 248
 Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala
 1 5 10 15
 Gly Ala Asp Val
 20

<210> 249
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 249

Gly Phe Tyr Pro Ile Leu Asn Ala Thr Val Thr Ala Thr Val Glu Pro
 1 5 10 15
 Glu Thr Gly Asp
 20

<210> 250

<211> 20

<212> PRT

<213> Homo sapiens

<400> 250

Phe Asp Pro Asp Gly Arg Lys Tyr Tyr Thr Asn Asn Phe Ile Thr Asn
 1 5 10 15
 Leu Thr Phe Arg
 20

<210> 251

<211> 20

<212> PRT

<213> Homo sapiens

<400> 251

Leu Gln Ala Leu Lys Val Thr Val Thr Ser Arg Ala Ser Asn Ser Ala
 1 5 10 15
 Val Pro Pro Ala
 20

<210> 252

<211> 153

<212> PRT

<213> Homo sapiens

<400> 252

Met Ala Ser Val Arg Val Ala Ala Tyr Phe Glu Asn Phe Leu Ala Ala
 1 5 10 15
 Trp Arg Pro Val Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val
 20 25 30
 Pro Met Gly Asp Val Pro Met Asp Gly Ile Ser Val Ala Asp Ile Gly
 35 40 45
 Ala Ala Val Ser Ser Ile Phe Asn Ser Pro Glu Glu Phe Leu Gly Lys
 50 55 60
 Ala Val Gly Leu Ser Ala Glu Ala Leu Thr Ile Gln Gln Tyr Ala Asp
 65 70 75 80
 Val Leu Ser Lys Ala Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr
 85 90 95
 Pro Glu Ala Phe Glu Lys Leu Gly Phe Pro Ala Ala Lys Glu Ile Ala
 100 105 110
 Asn Met Cys Arg Phe Tyr Glu Met Lys Pro Asp Arg Asp Val Asn Leu
 115 120 125
 Thr His Gln Leu Asn Pro Lys Val Lys Ser Phe Ser Gln Phe Ile Ser
 130 135 140
 Glu Asn Gln Gly Ala Phe Lys Gly Met
 145 150

<210> 253
 <211> 462
 <212> DNA
 <213> Homo sapiens

<400> 253
 atggccagtg tccgcgtggc ggcctacttt gaaaactttc tcggcgcggtg gcggcccggtg 60
 aaagcctctg ttccgagatta ctacaccttg gctgtaccga tgggagatgt accaatggat 120
 ggatatctctg ttgctgatata tggagcagcc gtctctagca tttttaattc tcacagaggaa 180
 tttttaggca aggcgctggg gctcagtgca gaagcactaa caatacagca atatgctgat 240
 gttttgtcca aggcctttggg gaaagaagtc cgagatgcaa agattacccc ggaagctttc 300
 gagaagctgg gattccctga agcaaaaggaa atagccaata tgtgtcgttt ctatgaaatg 360
 aagccagacc gagatgtcaa tctcaccac caactaaatc ccaagtgcaa aagcttcagc 420
 cagtttatct cagagaacca gggagccttc aagggcagt ag 462

<210> 254
 <211> 8031
 <212> DNA
 <213> Homo sapiens

<400> 254
 tggcgaaatg gacgcgcctt gtagcggcgc attaaagcgc gcgggtgtgtg tggttacgcg 60
 cagcgtgacc gctacacttg ccagcgccct agcgcccgct cctttcgctt tcttcccttc 120
 cttctctgcc acgttctgcc gctttccccc tcaagctcta atcgggggc tcctcttagg 180
 gttcgtattt agtcttttac ggcacctcga ccccaaaaaa cttgattagg gtgatgttct 240
 acgtagtggg ccactgcctc gatagacggt ttttcgcctc ttgacgttgg agtccacgtt 300
 ctttaatagt ggactcttgt tccaaacttg acaaacactc aacccattct cggctctattc 360
 ttttgattta taagggaatt tgcgatttc ggccatttgg ttaaaaaatg agctgattta 420
 acaaaaattt aacgcgaatt ttaacaaaat attaacgttt acaatttcag gtggcacttt 480
 tcggggaaat gtgcgcggaa cccctatttg tttatttttc taaatgtaac caaatatgta 540
 tcgcgtcatg aattaattct tagaaaaact catcgagcat caaatgaaac tgcaatttat 600
 tcatatcagg attatcaata ccataatttt gaaaaagcgc tttctgtaat gaaggagaaa 660
 actcaccgag gcagttccat aggatggcaa gatcctggtt tcggtctgcg attccgactc 720
 gtccaacatc aatacaacct attaatctcc cctcgtcaaa aataaggtta tcaagtgaga 780
 aatcaccatg agtgacgact gaatccgggt agaattggcaa aagtttatgc attcttttcc 840
 agacttgttc aacaggccag ccaattacgt cgtcatcaaa atcaactcga tcaaccaaac 900
 cgtttatcat tcgtgattgc gctgagcga gacgaaatac gcgatcgtcg ttaaaaggac 960
 aattacaacc aggaatcgaa tgcaaccggc gcaggaacac tggccagcga tcaacaatat 1020
 ccttccatga atcagattat tottctaata cctgggaatgc tgttttccgc gggatcgcaag 1080
 tgggtgagtaa ccaatgcata tcaggagtac ggataaaaatg cttgatgttc ggaagagcca 1140
 taaattccgt cagccagttt agtctgacca totcatctgt aacatcaattg gcaacgctac 1200
 ctttgcgatg tttcagaaac aactctggcg catcgggctt ccatatacaat cgatagattg 1260
 tcgcacactg ttccgcgcga ttatcgcgag cccattttata ccatataaaa tcagcatcca 1320
 tgttgggaatt taatcgcgcg ctagagcaag acgttttccg ttaaatatg ctcaatacac 1380
 cctctgtatt acgtttttatg taagcagaca gttttattgt tcatgaccaa aatcccttaa 1440
 ccgtgatttt cgttccactg agcgtcagac ccgctagaaa agatcaaaag atctcttcta 1500
 gatccttttt ttctgcgcgt aatctgtctg ttgcaaaaca aaaaaccacc gctcacagcg 1560
 gtggtttgtt tgccgataca agagctacca actctttttc cgaagtgtac tggcttcagc 1620
 agagcgca taccaaaatac tgtccttcta gtgtagccgt agtttagcca caacttcaag 1680
 aactctgata caccgcctac atacctcgt ctgtataatc tgttaccagt ggctgtgcgc 1740
 agtggcgata agtcgtgtct tacogggttg gactcaagac gatagtacc ggataaggcg 1800
 cagcggctgg gctgaacggg gggttcgtgc acacagccca ccttggagcg aacgacctac 1860
 accgaactga gatacctaca gcttgagcta tgaaaaggcg ccagcttcc cgaaggaga 1920
 aaggcggaca ggtatccggt aagcggcagg gtccggaacg gagagcgac gagggagctc 1980
 ccagcgggaa acgcgggtga tctttatagt cctgtcgggt ttgccacact ctgacttgag 2040
 cgtcgtattt tgtgatgctc gtacgggggg cggagcctat ggaaaaacgc cagcaacgcg 2100
 gcctttttac ggttccctgc cttttgtctg ccttttgcgc acatgttctt tctcgcgtta 2160

tcccttcgatt	ctgttgataa	cgttattacc	gcctttgagt	gagctgatac	cgtcgcgcgc	2220
agccgaacag	ccgagccgag	cgaagtacgt	agcgaggag	cggaagagcg	ctgtagcgcg	2280
tatttttccc	ttacgcactc	gtcgcgtatt	tcacaccgca	tatatggtcg	actctcagta	2340
caatctgcct	tgatgcgcga	tagttaagcc	agtatacact	ccgctatcgc	tacgtgactg	2400
ggctcatggct	gcgcgccgac	accgcgccac	accgcgtgac	ggccctcgac	gggcttgcct	2460
gtcccccggca	tcgcgttaca	gacaagctgt	gacgctctcc	gggagctgca	tgtgtcagag	2520
gttttccacc	tcattaccga	aacgcgcgag	gcagctgcgg	taaaagctcat	cagctgggctc	2580
gtgaagcgat	tcacagatgt	ctcgcgtctc	atccgcgtcc	agctcgttga	gtttctccag	2640
aagcgtttaa	gtctggctgt	tgataaagcg	ggccatgta	aggcgctgtt	tttctcgtgt	2700
gcgcactgat	gcctccgtgt	aagggggatt	tctgttcatg	ggggtaatga	taccgatgaa	2760
agcagagagg	atgtctacga	tacgggttac	tgatgatgaa	catgcccggt	tactcgaaag	2820
ttgtgagggg	aaacaactcg	cgttatggat	gcgcgcggac	cagagaaaaa	tcaactcagg	2880
tcaatgccag	cgcttcgtta	atacagatgt	aggtgttcca	cagggtagcc	agcagcatcc	2940
tgcgatgcag	atccggaaaca	taattggtgca	ggcgcgtagc	ttccgctgtt	ccagacttta	3000
cgaacacgca	aaacogaaaga	ccattcatgt	tgttgctcag	gtcgcagacg	ttttgcagca	3060
cgactcgctt	cacgttcgct	cgcgtatcgg	tgattcatte	tgctaaccag	taaggcaaac	3120
cagcagccct	agccgggtcc	tcacagacag	gagcacgata	atgcgcaccc	gtggggcgcc	3180
catccggcag	ataatggctc	gcttctcgcc	gaaaacgtttg	gtggcgggag	cagtagcagaa	3240
ggcttgagcg	agggcgtgca	agattccgaa	taccgcaagc	gacaggcgca	tcacgtctgc	3300
gtccacagcg	aacgggtctct	cgccgaaaat	gaccacagac	gtcgcgcgca	ctgtctctac	3360
gagttgcatg	ataaagaaga	cagtcataag	tgccggcagc	atagtcacgc	cccgccgcca	3420
ccgggaaggag	ctgactgggt	tgaagggctc	caagggcatc	ggtcgagatc	ccggtgccata	3480
atgagtgagc	taactctaac	taattgcgtt	gcgctcaact	cccgctttcc	actcgggaaa	3540
cttgcctgctg	cagctgcatt	aatgaatcgg	ccaacgcgcg	gggagaggcg	gtttgcgtat	3600
cgggtcgctt	gggtggtttt	cttttcacca	gtgagacggg	caacagctga	ttgcctctca	3660
ccgcctggcc	ctgagagagt	tgacgcaagc	ggttccacgt	ggtttgcccc	agcaggcgaa	3720
aatctgtgtt	gactgtgtgt	aacggcgggg	tataacatga	gctgtcttcg	gtatcgttgt	3780
atcccaactac	cgagataatcc	gcaccaacgc	gcagcccgga	ctcggttaatg	gcgcgcattg	3840
cgccacgcgc	catctgatcgt	ttggcaacca	gcacgcagct	gggaacagatg	ccctacttca	3900
gcatttgcat	ggtttgttga	aaacoggaca	tggaactcca	gtcgccttcc	cgttccgcta	3960
tcggctgaat	ttgattgoga	gtgagatatt	tatgccagcc	agccagagcc	agacggcccg	4020
agacagaact	taattggccc	gctaacacgc	cgatttgcgt	gtgacccaat	gcgaccagat	4080
gtccacagcc	cagtcgcgta	ccgtcttcat	gggagaaaaa	aatactgttg	atgggtgtct	4140
ggtcagagac	atacgaanaa	aacgcgggaa	cattagtcca	ggcagcttcc	acagcaatgg	4200
catccttggt	atccagcgga	tagttaatga	tcagcccaact	gacgcgttgc	gcgagaagat	4260
ttgtcagcgc	gcctttacag	gcttcgacgc	cgcttctgtt	taccatcgac	accaccaagc	4320
tgccacccag	ttgatcgcg	cgagatttaa	tcgccgcgac	aatttgcgac	ggcgcgctga	4380
ggagcagact	ggaggtggca	acgccaaatc	gcaacagact	tttgcgccgc	agtttgttgt	4440
ccacgcggtt	gggaatgtaa	ttcagctccg	ccatcgccgc	ttccaatttt	ttccgcgttt	4500
tcgcagaaac	gtggctggcc	tggttcacca	cgccgggaac	gggtcgataa	gagacacccg	4560
cataactctgc	gaactctgat	aacgttactg	gtttcaactt	ccaccacccg	aattgactct	4620
cttcgcggcg	ctatcatgcc	ataccggcaa	aggtttttgc	ccattcgatg	gtgtccggga	4680
tttcgcagct	ctcccttatg	cgactccctg	attaggaagc	agccccagtag	taggtttaggt	4740
ccgttgagca	cgccgcgcgc	aaggaaatgt	gcgatgcaag	agatggcgcc	caacactccc	4800
cgccgcacgc	ggcctccca	cataccagc	ccgaaacaag	cgctcatgag	ccogaagtgc	4860
cgagcccgat	cttcccccac	ggtgatgtcg	gcgatatagg	cgccagcaac	cgccactctg	4920
gcgcgcgtga	gtccgcgcac	gatgcgtccg	gcgtagagga	tcgagatctc	gatcccgcca	4980
aatttaatac	actcactata	gggggaattg	gagcggataa	caattccctt	ctagaaataa	5040
ttttgtttaa	ctttaagaag	gagatataca	tatgcagcat	caccacccat	accacggagt	5100
acagcttcaa	gaactagggt	ataatggatt	gctcatgca	ataatccctc	aggtacctga	5160
gaatcagaa	ctcatctcaa	acattaagga	aatgataact	gaagcttcat	tttaccattt	5220
taattctacc	aagagaagag	tatttttcag	aaataataac	attttaaatc	ctgcacatgt	5280
gaagcctaag	aataaacgca	aaataaaaca	agaatcatat	gaaaaggcaa	atgtcatagt	5340
gactgactgc	tatggggcac	atggagatga	tcacataacc	ctacataaca	gaggggtgtg	5400
aaaaagagga	aaatacattc	atttccaccc	taatttctta	ctgaatgata	acttaacagc	5460
tggtctacga	tcaagaggcc	gagtggttgt	ccatgaatgg	gcccaactcc	gttgggggtg	5520
gttcgatgat	tataacaatg	acaaaccttt	ctacataaat	ggggcaaatc	aaattaaagt	5580
gacaagggtg	tcatctgaca	tcacaggcat	ttttgtgtgt	gaaaaaggct	cttgccecca	5640

```

agaaaactgt attattagta agcttttttaa agaaggatgc acctttatct acaatagcac 5700
ccaaaatgca actgcacataa taatgtttcat gcaaaagtta tcttctgtgg ttgaattttg 5760
taatgcaagt acccacaacc aagaagcacc aaacctacag aaccagatgt gcaagcctcag 5820
aagtgcatgt gatgtaatca cagactctgc tgactttcac cacagotttc ccatgaacgg 5880
gactgagctt ccaacctctc ccacattctc gcttgtagag gctgggtgaca aagtggctgt 5940
tttagtgctg gatgtgtcca gcaagatggc agaggctgac agactccttc aactacaaca 6000
agccgagtaa ttttatttga tgcagattgt tgaattcoat acctctgtgg gcatgtgccg 6060
tttcgacagc aaaggagaga tcagagccca gctacaccaa attaacagca atgtatgatc 6120
aaagtgtgtg gtttcatatc tgcccaccac tgtatcagct aaaaacagaca cagacttttg 6180
ttcaggggctt aagaagaagt tttaggttgt tgaaaaaact aatggaanaa cttatggctc 6240
tgtgatgata tttagtgcca gcggagatga taagcttctt ggcaatttgc taccocattg 6300
gctcagcagt ggttcaacaa ttcaactccat tgccctgggt tcaatctgca ccccaaatct 6360
ggaggaatta tcacgtctta caggagggtt aaagtctctt gttccagata tatcaaacct 6420
caatagcatc attgatgctt tcagttagaatt ttcctctgga actggagaca ttttccagca 6480
acatatcagc cttgaaagta caggtgaaaa tgtcaaacct caccatcaat tgaanaaacac 6540
agtgactgtg gataatactg tgggcaacga cactatgttt ctagttagct ggccggccag 6600
tggctctctc gagattatat tatttgatcc tgatggacga aaatactaca caataaattt 6660
tatccacaaat ctaacttttg ggacagctag tcttttgatt ccaggaaacag ctaagcctgt 6720
gcactggact tacaccctga acaataccca tcaattctct caagccctga aagtgacagt 6780
gacctctcgc gctctcaact cagctgtgcc cccagccact gtgggaagcct ttgtggaaag 6840
agacagcctc cactttcttc atcctgtgat gatttatgcc aatgtgaac agggatttta 6900
tccacttctt aatgccact tcactgccac agttgagcca gagactgga acctctgtac 6960
gctgagactc cttgatgatg gagcagggtc tgatgttata aaaaatgatg gaatttactc 7020
gaggtatttt ttctcctttg ctgcaaatgg tagatatagc ttgaaagtgc atgtcaatca 7080
ctctcccagc ataagcacc cagccactc tattccaggy agtcatgtcta tgtatgtacc 7140
aggttacaca gcaaacgcta atattcagat gaatgtccca aggaatcagc taggcagaaa 7200
tgagagctag cgaaagtggg gcttttagcg agtcagctca ggaagctcct ttccagtgtc 7260
gggagttcca gctggccccc accctgatgt gtttccacca tgcataaata ttgaccttga 7320
agctgtaaaa gttagaagaa aattgacctt atcttggaca gcacctggag aagactttga 7380
tcagggccag catcaacgct atgaaataag aatgagtaaa agtctacaga atatccaaga 7440
tgactttaac attgctattt tagtaaatat atcaaaagcga aatcctcagc aagctggcat 7500
caggggagata ttacgtttct caccocaaat ttccacgaat ggacctgaac atacgccaaa 7560
tggagaaaca catgaaagcc acagaattta tgttgcaata cgagcaatgg ataggaaact 7620
cttacagctc gctgtatcta acattgcccc ggogcctctg tttattccoc caaattctga 7680
tctgtacctt gccagagatt atcttatatt gaaaggagtt ttaacagcaa tgggtttgat 7740
aggaatcatt tgctttatta tagttgtgac acatcatact ttaagcagga aaaaagagagc 7800
agacaagaaa gagaatggaa caaaatttat ataatgaatt ctgcagatat ccatcacact 7860
ggcgccgctc cgagcaccac caccaccacc actgagatcc ggctgtcaac aaagcccgaa 7920
aggaagctga gttggctgct gccaccgctg agcaataact agcataaacc cttggggcct 7980
ctaaacgggt cttgaggggt tttttgctga aaggaggaa c tatatccga t 8031

```

<210> 255

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 9, 67, 247, 275, 277, 397

<223> n = A,T,C or G

<400> 255

```

gtggccagng actagaaggc gagggccgcg gggaccatgg cggcgccggc ggacgagcgg 60
agtcnaanag acggagaaga cgaggagaag gagggacagt tggttctggt ggaattatca 120
ggaattattg attcagactt cctctcaaaa tgtgaaaata aatgcaaggt ttggggcatt 180
gacactgaga ggccattctt gcaagtggac agctgtgtct ttgctgggga gtatgaagac 240

```

```

actctangga cctgtgttat atttgaagaa aatgntnaac atgctgatac agaaggcaat 300
aataaaaacag tgctaaaata taaatgccat acaatgaaga agctcagcat gacaagaact 360
ctctcgacag agaagaagga aggagaagaa aacatangtg g 401

```

```

<210> 256
<211> 401
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 7, 37, 51, 79, 96, 98, 103, 104, 107, 116, 167, 181, 183,
194, 206, 276, 303, 307, 308, 310, 323, 332, 341, 353, 374,
376
<223> n = A,T,C or G

```

```

<400> 256
tggtggncct gggatgggga accgcgggtg cttccngnga gggttcggca ntggcatccg 60
gggcccgggt cgccggcgng gacggggccg gggccnango cgnnganctc gcggangcaa 120
ggccaggagat aaggagtga tgcccgctcac caacttgggc cgcttgncca aggacatgaa 180
nancaagccc ctgnaggaga tctatntctt cttccctgcc ccattaaagga atcaagagat 240
catttgattt cttcctgggg gctctctcea aggatnaggt tttgaagat tatgccagt 300
canaaannan accccgttgc ccngtccatc tncacccaac ncttcaaagg gcnatttttg 360
tttaggcctc attnncgggg ggaaccttaa cccaatttgg g 401

```

```

<210> 257
<211> 401
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 382, 387
<223> n = A,T,C or G

```

```

<400> 257
atgtatgttaa aacacttcat aaaatgtaaa gggctataac aaatatgtta taaagtatt 60
ctctcagccc tgagggtatac agaatcattt gcctcagact gctgttgtag tttaaaattt 120
ttaaaaatct tgctaagtaa ttgtctatgt cttctcccac actatcaata tgcotgcttc 180
taacaggctc cccactttct tttaatgtgc tgttatgagc tttggacatg agataaacgt 240
gctctgttcag agtgtctaca gtaagagctg gacaaactct ggagggacac agtcttttag 300
acagctcttt tgggttgttt ccacttttct gaaaggttca cagtaacott ctagataata 360
gaaactccca gttaaagcct angctancaa ttttttttag t 401

```

```

<210> 258
<211> 401
<212> DNA
<213> Homo sapiens

```

```

<400> 258
ggagcgctag gtcggtgtac gaccgagatt aggtgtcggt ccagctccgg gaggcccgcg 60
tgaggggccg ggcccagct gccgaccga gccgatcgct aggtgtcgca gcgctcagc 120
ctctgtggag agcagcagta gtcggagggt gcaggatatt agaaatggct actccccagt 180
caattttcat ctttgcaatc tgcattttaa tgataacaga attaattctg gcctcaaaaa 240
gtactatga tatcttaggt gtgccaaaat cggtatcaga gcgccaaatc aagaaggcct 300
ttcacagatt ggccatgaag taccaccctg acaaaaaata gaccagatg ctgaagcaaa 360
attcagagag attgcagaag catatgaaac actctcagat g 401

```

```

<210> 259
<211> 401
<212> DNA
<213> Homo sapiens

<400> 259
attgggtttg gagggaggat gatgacagag gaatgccctt tggccatcac ggttttgatt 60
ctccagaata ttgtgggttt gatcatcaat gcagtcatgt taggctgcat ttatcatgaa 120
acagctcagg ctacagaag ggcagaaact ttgatattca gccgccatgc tgtgattgcc 180
gtccgaatg gcaagctgtg ctccatgttc cgagtgggtg acctgaggaa aagcatgato 240
attagtgcct ctgtgcgcac ccaggtgttc aagaaaacaa ctacacctga aggggaggtg 300
gttcctattc accaactgga cattcctgtt gataacccaa tcgagagcaa taacattttt 360
ctgtgggcc ctatgatcat ctgccacgtg attgacaagc g 401

<210> 260
<211> 363
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 7, 9, 19, 41, 63, 73, 106, 111, 113, 116, 119, 156, 158,
162, 187, 247, 288, 289, 290, 292, 298, 299, 300, 340
<223> n = A,T,C or G

<400> 260
aggaganang gagggggana tgaataggga tggagaggga natagtggat gaggcaggca 60
canggagagg aancagaaag gagaggcaag acagggagac acacancaca nangangana 120
caggtggggg ctgggggtgg gcattggagag cctttnangt cncocaggcc accctgctct 180
cgctggngctg ttgaaaccca ctccatggct tcttgccact gcagttgggc ccagggctg 240
cttatnctg gaatgcaagt ggcctgtgct tggagcctcc cctctgmnng anggaaannn 300
attgtccctc tatctgcttg gaatatctga gtttttccan cccggaaata aaacacacac 360
aca 363

<210> 261
<211> 401
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 114, 152
<223> n = A,T,C or G

<400> 261
cggtctctcc cgctctctcc ggggttttcg ggcacttggg tcccacagtc tggctctgct 60
tcaccttccc ctgacctgag tagtcgccat ggcacagggt ctacagaggca ctgnactga 120
cttcctctga ttgatgagc ggcctgatgc anaaactctt cgaagggcta tgaaggtct 180
gggacagagt gaggagagca tctgactct gttgacatcc ogaagtaatg ctacgcgcca 240
gaaatctct gcagctttta agactctgtt tggcagggat cttctgagat acctgaaatc 300
agaaactaac ggaaaattg aaaaattaat tgtggctctg atgaaacctc ctgcgcttta 360
tgatgcttat gaactgaaac atgccttgaa gggagctgga a 401

<210> 262
<211> 401
<212> DNA
<213> Homo sapiens

```



```

<220>
<221> misc_feature
<222> 7, 26, 258, 305, 358, 373, 374, 378
<223> n = A,T,C or G

<400> 262
agtctanaaac atttctaata ttttgngcgtt toatatatca aaggagatta tgtgaaacta 60
tttttaaaata ctgtaaagtgt acatatagtt ataagatata tttctgtaca gtagagaaag 120
agtttataaac atgaagaata ttgtaccatt atacattttc attctcgatc tcataagaaa 180
ttcaaaagaa taatgataga ggtgaaaata tgtttacttt ctctaaatca agcctagtgt 240
tcaactcaaaa aattatnntg catagtttta ttttgaattt aggttttggg actacttttt 300
tccancttca atgagaaaat aaaatctaca actcaggagt tactacagaa gttctaanta 360
tttttttgct aannagcnaa aaatataaac atatgaaaaa g 401

<210> 263
<211> 401
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 232, 290, 304, 326, 383
<223> n = A,T,C or G

<400> 263
ctgtccgacc aagagaggcc gccgcagccc gaggtctggg cttttgcttt ctggcgagg 60
gatctgcggc gatttaggag gccgcgctga tcttgggagg aagaggcagc tacggcgggc 120
gcggcggtgg cggctagggc gccgcgcaat aaaggggccc ccgcccgggtg atgcggtgac 180
cactgcggca gccccaggag ctgagtgggc cccggccctc agcccgtccc gncggaccgg 240
ctttcctcaa ctctccatct tctcctgcgc accgagatcg ccgaggcggn ctcaggctcc 300
ctancccttt ccccgctcct tcccncccc cgtcccgcgc ccggggggcg ccgccaccgg 360
cctcccacca tggctctgaa ganaatccac aaggaattga a 401

<210> 264
<211> 401
<212> DNA
<213> Homo sapiens

<400> 264
aacaccagcc actccaggac ccctgaaggc ctctaccagg tcaccagtg tctgcgccta 60
aagccacccc ctggcagaaa ctccagctgt gtgtttctgga atactcacgt gagggaaact 120
actttggcca gcattgacct tcaaaagttag atggaaccca ggaccatcc aacttggctg 180
tctcacattt tcatcccttc ctgcacatatt gctttcattt tcatagccac agtgatagcc 240
ctaagaaaac aactctgtca aaagctgtat tcttcaaaag acacaacaaa aagacctgtc 300
accacaacaa agaggggaagt gaacagtgt gtgaatctga acctgtggtc ttgggagcca 360
gggtgacctg atatgacatc taaagaagct tctgactct g 401

<210> 265
<211> 271
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 59
<223> n = A,T,C or G

<400> 265

```

```

gccacttcc  gtggacatgg  gcagagcgct  gctgccagtt  cctggtagcc  ttgaccacna  60
cgctgggggg  tctttgtgat  ggtcatgggt  ctcatttgca  cttgggggtg  tgggattcaa  120
gttagaagtt  tctagatctg  gccggggcca  gtggctcaca  cctgtaatcc  caggacttta  180
ggaggtctgag  gcaggcggtg  catgaggtca  ggagatcgag  accgtcctgg  ctaacacagt  240
gaaacccogt  ctctactaaa  aatacaaaaa  a
gaaacccogt  ctctactaaa  aatacaaaaa  a  271

```

```

<210> 266
<211> 401
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 45
<223> n = A,T,C or G

```

```

<400> 266
attcataaat  tttagctgaaa  gatactgatt  caatttgtat  acagngaata  taaatgagac  60
gacagcaaaa  ttttcatgaa  atgtaaaata  tttttatagt  ttgttcatac  tatatgaggt  120
tctatttttaa  atgactttct  ggatttttaa  aaatttcttt  aaatacaatc  atttttgtaa  180
tatttatttt  atgcttatga  tctagataat  tgcagaatat  cattttatct  gactctgtct  240
tcataagaga  gctgtggccg  aattttgaac  atctgttata  gggagtgtac  aaattagaag  300
gcaatgtgga  aaaacaatto  tgggaaagat  ttctttatat  gaagtccttg  ccaactagcca  360
gccatcctaa  ttgatgaaa  ttatctgttc  acaggcctgc  a
gccatcctaa  ttgatgaaa  ttatctgttc  acaggcctgc  a  401

```

```

<210> 267
<211> 401
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 116, 247, 277, 296, 307, 313, 322, 323, 336, 342, 355, 365,
377, 378, 397
<223> n = A,T,C or G

```

```

<400> 267
gaagaggcat  cacctgatcc  cggagacctt  tggagttaag  aggcggcgga  agcggaggcc  60
tgtggagtcg  gatcctcttc  ggggtgagcc  agggctggcg  cgccggcgctg  tctcanaact  120
catgcagctg  ttcccgcgag  gcctgtttga  ggaacgcgtg  ccgcccatcg  tgotgaggag  180
ccaggtgtac  agccttgtgc  ctgacaggac  cgtggccgac  cgccagctga  aggagcttca  240
agagcagggg  gagacaaaat  cgtccagctg  ggcttcnaact  tggatgccca  tgggaattat  300
tctttccttt  ganggactta  cnnngggacc  aagaanccct  tnaaaggggc  ccttngtgga  360
tggngnccga  aaccccnnta  ttgtgccttg  ggggggncca  a
tggngnccga  aaccccnnta  ttgtgccttg  ggggggncca  a  401

```

```

<210> 268
<211> 223
<212> DNA
<213> Homo sapiens

```

```

<400> 268
tgcctatgtt  ggccaggctg  gtcttgaact  cctgacttta  agtgatccac  ccgcctcaac  60
ctcccaagtt  gctgggatta  caggtgtgag  ccacgcgcgc  tggcctgata  catactttta  120
gaatcaagta  gtcacgactt  tttctgttcc  atttttctaa  aaagtaataa  tacaaatgtt  180
ttgttttttt  tttttttttt  ttgtttgttt  ctgttttttt  ttt
ttgttttttt  tttttttttt  ttgtttgttt  ctgttttttt  ttt  223

```

```

<210> 269
<211> 401

```

<212> DNA

<213> Homo sapiens

<400> 269

```

actatgtaaa ccacattgta ctttttttta ctttggaac aaatatttat acatacaaga 60
tgotagtcca ttgtaatat tctcccaact tatccaagga tctccagctc taacaaaatg 120
gtttattttt atttaaatgt caatagtgtt tttttaaaaa ccaaatcaga ggtgcaggcc 180
accagttaaa tgcgctctat caggttttgt gcccttaagag actacagagt caaagctcat 240
ttttaaagga gttaggacaaa gttgtcacag gtttttgttg ttgtttttat tgcccccaaa 300
attacatggt aatttcattt tatatcaggg attctattta cttgaagact gtgaagttgc 360
cattttgtct cattgttttc ttgacataa ctaggatcca t 401

```

<210> 270

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 240, 382

<223> n = A,T,C or G

<400> 270

```

tggctgttga ttcaacctcag cactgcttgg tatctgcacc ctacctctct ttagaggctg 60
ccttgtcaac tgaaaaatgc acctgacttc gagcaagact ctttccttag gttctggatc 120
tgttttagacc coactggcact gagctggaat ctgagggctc tgttccaagg atgtgatgat 180
gtgggagaat gttctttgaa agagcagaaa tccagctctgc atggaaacag cctgtagagn 240
agaagtttcc agtgataagt gttcactggt ctaaggaggt acaccacagc tacctgaatt 300
ttcccaaaat gagtgtctct gtgcgttaca actggccttt gtacttgact gtgatgactt 360
tgttttttct tttaattctc anataaacat gggaaaaaat g 401

```

<210> 271

<211> 329

<212> DNA

<213> Homo sapiens

<400> 271

```

ccacagcctc caagtacagt ggggtggagt cccagagctg cacagggttt ggccaaagt 60
tctaaggagg gcacttcttc ccttcgcccc tcagtgccag cccctgctgg ctggtgcctg 120
agccctcagc acagcccctc gccocgcagg cctgccttct cagggacttc tgccggggcct 180
gaggcaagcc atggagttag acccaggagc cggacacttc tcaggaaatg gcttttccca 240
acccccagcc cccaccgggt ggttcttctc gttctgtgac tgtgtatagt gccaccacag 300
cttatggcat ctcattgagg acaaaaaaa

```

<210> 272

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

```

<222> 1, 7, 12, 21, 61, 62, 66, 72, 78, 88, 90, 92, 98, 117, 119,
128, 130, 134, 142, 144, 151, 159, 162, 164, 168, 169, 177,
184, 185, 188, 194, 202, 204, 209, 213, 218, 223, 231, 260,
272, 299, 300, 306, 321, 322, 323, 331, 335, 336, 338

```

<223> n = A,T,C or G

<221> misc_feature

<222> 341, 342, 343, 345, 346, 351, 358, 360, 362, 363, 387, 390,
392

<223> n = A,T,C or G

<400> 272
 nggctgntaa cntcggaggt nacttctctgg actatcctgg agaccocctc cgcttccacg 60
 nncatnatat cncctcatngc tgggcccntn angacacnat cccactccaa cacctgngng 120
 atgctgngcn cctnggaaco ancntcagaa ngaccctgnt cntntgtntnt ccgcaantcg 180
 aagntaaangc gggntacacc tncntgcant ggnccacnct gcnggggaact ntacacacct 240
 acgggatgtg ctgcgcocan gagccaaagag cntttcttga tgattcccca gcctcttgnn 300
 agggantcta caacattgct nntacacctt ntcnncnctg nntntntgga ntacagngnn 360
 tnttaacact acatcttttt tactgcncnct tnccttggtgg g 401

<210> 273

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 399

<223> n = A,T,C or G

<400> 273
 cagcaccatg aagatcaaga tcatcgaccc ccagagagcgc aagtactcgg tgtggatcgg 60
 tggctccatc ctggcctcac tgtccacctt ccagcagatg tggattagca agcaggagta 120
 cgacgagtcg ggcccoctcca tegtccacog caaatgcttc taaacggact cagcagatgc 180
 gtgactatgt ctgcgatgggt taattagagaa tagaaatttg ccctcgacaa atgcacacac 240
 ctcatcgtag cctcacgaaa ctggaataag ccttcgaaaa gaaattgtcc ttgaagcttg 300
 tatctgatat cagcaactgga ttgtagaact tgttgctgat ttgaaccttg tattgaagtt 360
 aactgttccc ctgtgtatta acgtgtcagg gctgagtgt c 401

<210> 274

<211> 401

<212> DNA

<213> Homo sapiens

<400> 274
 ccaccacac ccaccgcgc ctgcttcgcc tcttctccgg gagccagtc gcgcacccgc 60
 gcgcgccagc gccatcgcca cctccgcgag ccattgtccc cagggtccgt tctctgtcct 120
 cctaccgcag gatgttggcg ggcccgggca ccgcgagccg ccgagactcc agccggagct 180
 acgtgaactac gtccacccgc acctacagcc tgggcagcgc gctgcgcccc agcaccagcc 240
 gcagcctcta cgctcgttcc ccggcgcgcg tgtatgccac gcgctcctct ccctgcgcgc 300
 tgcggagcag cgtgcccgcg gtgcggtcc tgcaggactc ggtggacttc tcgctggccg 360
 acgcacatcaa caccgagttc aagaacaccc gcaccaacga g 401

<210> 275

<211> 401

<212> DNA

<213> Homo sapiens

<400> 275
 ccacttcac cactttgtgg agcagtgctt tcagcgcaac ccgagtgcca ggtatccctg 60
 ctggcctcgg ctgggcttcc gggagagcag aggggtctca ggagggtaag gccaggggtg 120
 gaaggagact acctcccaaa ggttctcgag ggaatctcgg agctacacac agggagggatc 180
 agctcctcgg ttgtgcagag gccagcctgg ggaagctcgg ccactgcttc ccagagctg 240
 agggagaggg agaggggacc cgaggctcag gcataagtgg caggatttcg ggaagctggg 300
 gacacggcag tgatgtctgg gtctctcttc ccttttccct ccaggccagc tgccagcacc 360

ctcctgaacc actcttttctt caagcagatc aagcgacgtg c 401

<210> 276

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 11

<223> n = A,T,C or G

<400> 276

```
tctgatattg ntacccttga gccacctaaag ttagaagaaa ttggaaatca agaagttgtc 60
attgttgaag aagcacagag ttccagaagac tttaacatgg gctcttcttc tagcagccag 120
tatactttct gtccagccaga aactgtattt tcatctcagc ctagtgtatga tgaatcaagt 180
agtgtatgaaa ccagtaataca gcccagtcct gccctttagac gacgcgcgtgc taggaagaag 240
accgtttctg ctccagaatc tgaagaccgg ctagtgtgtg aacaagaaac tgaaccttct 300
aaggagttga gtaaacgtca gttcagtagt ggtctcaata agtgtgttat acttgccttg 360
gtgattgcaa tcagcatggg atttggccat ttctatggca c 401
```

<210> 277

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 227, 333

<223> n = A,T,C or G

<400> 277

```
aacttttgca acatatctca gcaaaaacta cagctatgtt attcatgcc aataaaaagc 60
tgtgcagagg agtggctgca atgaggtcac aacggtgggt gatgtaaaag agatcttcaa 120
gtcctcatca cccatccctc gaactcaagt cccgctcatt acaaatctct cttgcccagt 180
tccacacatc ctgccccatc aagatgttct catcatgtgt tacgagnggc gctcaaggat 240
gatgcttctt gaaaattgct tagttgaaaa atggagagat cagcttagta aaagatccat 300
acagtgggaa gagaggctgc aggaacagcg ganaacagtt caggacaaga agaaaacagc 360
cgggcgcacc agtcgtagta atcccccaa accaaaaggga a 401
```

<210> 278

<211> 401

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 322, 354

<223> n = A,T,C or G

<400> 278

```
aatgagtggt agaccacaaa tgaatgccgg gaggatgaaa tgtgttgaa ttatcatggc 60
ggcttcogtt gttatccacg aaatccttgt caagatccct acattctaac accagagaac 120
cgatgtgttt gcccagcttc aaatgccatg tgccgagaac tgcccagtc aatagtctac 180
aaatacatga gcatccgata tgataggtct gtgccatcag acatcttcca gatacagggc 240
acaactattt atgcacaacac catcaatact ttctggatta aatctggaaa tgaacaatgga 300
gagtctacct acgacaacaa anccctgtaa gtgcaatgct tgtgtctgtg aagncattat 360
caggaccaag agaacatata gtggacctgg agatgctgac a 401
```

<210> 279
 <211> 401
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 30, 35, 81, 88, 180, 212, 378, 384, 391
 <223> n = A,T,C or G

<400> 279
 aaattattgc ctctgatata tacctaagtn aacanaacat taatacctaa gtaaacataa 60
 cattactctgg aggggttcag nttctaantg aaactgtatt tgaaactttt aagtatactt 120
 taggaacaaa gcatgaacgg cagtctagaa taccagaaac atctacttgg gtagcttggm 180
 gccattatcc tgtggaatct gatatgtctg gnagcatgtc attgatggga catgaagaca 240
 tcttttgaaa tgatgagatt atttcctgtg ttaaaaaaaa aaaaaatcct aaattcctac 300
 aatgtgaaac tgaaactaat aattttgata ctgatgtatg ggacagcgta tctgtaccoag 360
 gctctaaata acaaaagnta ggngacaag nacatgttcc t 401

<210> 280
 <211> 326
 <212> DNA
 <213> Homo sapiens

<400> 280
 gaagtggaaat tgtataatcc aattcgataa ttgatctcat gggctttccc tggaggaaag 60
 gttttttttt ttgttttttt ttaagaacct tgaaacttgt aaactgagat gtotgtagot 120
 tttttgccca tctgtagtgt atgtgaagat ttcaaaacct gagagcactt tttctttggt 180
 tagaattatg agaaaggcac tagatgactt taggatttgc atttttccct ttattgcccc 240
 atttcttgtg aocgcttgtt ggggagggaa atctgtttat ttttctacta aaataaaaaa 300
 ctaagattct atatcgcaaa aaaaaa 326

<210> 281
 <211> 374
 <212> DNA
 <213> Homo sapiens

<400> 281
 caacgcggtt gcaaatatcc ccttggttagc ctacttccct acccccgaat atttgtaaga 60
 tcgagcaatg gottcaggac atgggttctc ttctctctgt atcattcaag tgctcactgc 120
 atgaagactg cgttgtctca gtgtttcaac ctcaaccagg ctgtctcttg gtccacacct 180
 cgtccctgt tagtgccgta tgacagcccc catcaaatga ccttggccaa gtcaacggtt 240
 ctctgttgct aaggttggtt ggctgattgg tggaaagtag ggtggaccaa aggaggccac 300
 gtgagcagtc agcaccagtt ctgcaccagc agcgctccg tctagtggg tgttctctgt 360
 tctctctgsc ctgg 374

<210> 282
 <211> 404
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 26, 27, 51, 137, 180, 222
 <223> n = A,T,C or G

<400> 282

```

agtggtggtgg aattcccgca tcctanncgc cgactcacac aaggcagagt ngccatggag 60
aaaaattccag tgtcagcatt cttgctcctt gtggccctct cctacactct gggccagagat 120
accacagtcga aacctgnagc caaaaaggac acaaggact ctcgacccaa actgcccann 180
acctctccca gaggttgagg tgaccaactc atctggactc anacatatga agaagctcta 240
tataaatcca agacaagcaa caaacccctg atgattatct atcacttgga tgagtgccca 300
cacagtcgaag ctttaagaaa agtgtttgct gaaaataaag aaatccagaa attggcagag 360
cagtttgctc tcctcaatct ggtttatgaa acaactgaca aaca 404

```

```

<210> 283
<211> 184
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 26
<223> n = A,T,C or G

```

```

<400> 283
agtggtggtgg aattccacttg cttaanttgt gggcaaaaga gaaaaaaga gattgatcag 60
agcattgtgc aatacagttt cattaaatcc ttccctcgct cccccaataa ttigaatttt 120
tttttaacca ctcttacacc tggttatgaa aatgtcaacc tttgtaagaa aaccataata 180
aaaa 184

```

```

<210> 284
<211> 421
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 147, 149
<223> n = A,T,C or G

```

```

<400> 284
ctattaatcc tgccacaata tttttaatta cgtacaaaga tctgacatgt caccagggga 60
cccatttcac ccactgctct gtttggccgc cagtcttttg tctctctctt cagcaatggt 120
gaggcggata ccctttctct ggggaanana aatccatggt ttgttgccct tgccaataac 180
aaaagtgttg gaaagtcgag tggcgaagct gttgccaatt gcattcttca cgtgaaccac 240
gtcaaaagat ccagggtgcc tctctctggt ggtgatcaca ccaattcttc ctagggttagc 300
acctccagtc accatacaca ggtaaccagt gtgcgaactg atgaaatcag taactctgcc 360
agtctctaaa tcaatctgaa tggatatcatt caccttgatg aggggatcgg gtagcggat 420
g 421

```

```

<210> 285
<211> 361
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 34, 188
<223> n = A,T,C or G

```

```

<400> 285
ctgggtggta actctttatt tcattgtccg gaanaaagat gggagtggga acagggtgga 60
cactgtgcag gcttcagctt ccactccggg caggattcag gctatctggg accgcagggg 120
ctgccagggt cacagccctg gctcccaggg caggcaggga aggtgacggg actggaagcc 180

```

```

cttttcanag ccttggagga gctggtccgt ccacaagcaa tgagtgcac tctgcagttt 240
gcaggggatg gataaacagg gaaacaactgt gcattcctca cagccaacag tgtaggtctt 300
ggtgaagccc cggcgctgag ctaagctcag gctgttcacg ggagccacga aactgcaggt 360
a

```

<210> 286

<211> 336

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 40, 68, 75, 127, 262

<223> n = A,T,C or G

<400> 286

```

tttgagtggc agcgccctta tttgtggggg ccttcaagggn agggctgctgg ggggcagcgg 60
ggaggaanag ccganaaact gtgtgaccgg ggcctcaggt ggtgggcatt gggggctcct 120
cttgcanaatg cccatttgca tcaccggtgc agccattggt ggagcgggtt accggtcctt 180
tcttgtttcaa cataggggtag gtggcagcca cgggtccaac tcgcttgagg ctggggccctg 240
ggcgctccat tttgtgttcc angagcatgt ggttctgtgg cgggagcccc acgcagcggc 300
tgaggatggt ctcatgacag ctgcgctggc ggaaaa

```

<210> 287

<211> 301

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 15, 33, 44, 53, 76, 83, 107, 117, 154, 166, 192, 194, 207, 215, 241, 246

<223> n = A,T,C or G

<400> 287

```

tggggtaccaa attnttttat ttgaaggaat ggnacaaatc aaanaactta agnggatggt 60
ttgggtacaac ttatanaaaa ggnaaaggaa accccaacat gcatgcnctg ccttggngac 120
cagggaagtc accccaacggc tatgggggaaa ttancccgag gcttancctt cattatcact 180
gtctcccagg gngngcttgt caaaaaata ttccnccaag ccaaattcgg ggcgtcccat 240
nttgcnaaag ttggtcacgt ggtcacccaa ttctttgatg gctttcacct gctcattcag 300
g

```

<210> 288

<211> 358

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 39, 143, 226

<223> n = A,T,C or G

<400> 288

```

aagtttttaa acttttttatt tgcataattaa aaaaattgng cattccaata attaaaaatca 60
tttgaaacaaa aaaaaaatg gcactctgat taaactgcac tacagcctcg aggcacacct 120
gggccagctt ggtttttactc tanatttcac tgtcgtccca ccccacttct tccaccocac 180
ttcttctctc accaacaatgc aagttctttc ctctcctgcc agccanatag atagacagat 240
gggaaaggca ggcggcgctt tcgttgtcag tagttctttg atgtgaaaag ggcagcacag 300

```


tcattttaaac ttgatccaac ctctttgcat cttacaaagt taaacagcta aaagaagt 358

<210> 289

<211> 462

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 87, 141, 182, 220, 269, 327

<223> n = A,T,C or G

<400> 289

```

ggcatcagaa atgctgttta tttctctgct gctcccaagc tggctggcct ttgcagagga 60
gcagacaaca gatgcatagt tgggganaaa gggaggacag gttccaggat agagggtgca 120
ggctgaggga ggaagggtaa naggaaggaa ggccatcctg gatccccaca tttcagttct 180
anataggac aaagggactc ccaagccccc aaatcatcan aaaacaccaa ggagcaggag 240
gagcttgagc aggcoccagg gagcctcana gccataccag ccactgtcta cttcccatcc 300
tcctctccca ttcctgtctc gttctcanacc acctccagc taagccccag ctccattccc 360
ccaatcctgg cccttgccag cttgacagtc acagtgcctg gaattccacc actgaggctt 420
ctccagcttg gattaggagc tgcgccctgt agcatgtctc cc 462

```

<210> 290

<211> 481

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 44, 57, 122, 158, 304, 325, 352, 405

<223> n = A,T,C or G

<400> 290

```

tactttccta aactttatta aagaaaaaag caataagcaa tggnggttaa tctctanaac 60
atacccaatt ttctgggctt cctcccccga gaatgtgaca ttttgatttc caaacatgac 120
anaagtgtat ggttcccaac tgtactaaag taggtganaa gctgaagtcc tcaagtgttc 180
atcttccaac ttttccagct ctgtgtgtctg tcttttgatc agcaataatt gcctgaacag 240
ctactatggc ttctgtgatt tttgtctgta gctctctgag ctctctatg tgacgcaatc 300
gcanaaatttg agcagcttca ttaanaaact catctcctgt gtcaaaaacca anaatatgtt 360
tgtctaaagc aacaggtaag ccctcttttg tttgatttgc cttanaaact gcactcgtgt 420
tcaggcgctc ctgaacaaaa atccgaattg ccttaagcat taccaggtaa tcatcatgac 480
g 481

```

<210> 291

<211> 381

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 79, 166, 187, 208, 219, 315

<223> n = A,T,C or G

<400> 291

```

tcataagtaat gtaaaaccat ttgtttaatt ctaaaatcaa tcaactttcac aacagtgaaa 60
attagtactt ggtaaggng tgccactgta catatcatca tttctgactt ggggtcaagg 120
cctggtccta gtccacaagg gtggcaggag gaggggtgag gctaanaaca cagaaaacac 180
acaaaaanaa ggaaagctgc cttggcanaa ggatgaggng gtgagcttgc cgaaggatgg 240

```

```

tggaagggg gctccctgtt ggggcccagc caggagtcct aagtcagctc tcctgcctta 300
cttagctcct ggcanaagggt gagtggggac ctacgaggtt caaaatcaaa tggcatttgg 360
ccagcctggc ttactaaca g                                     381

```

```

<210> 292
<211> 371
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 32, 55, 72, 151, 189, 292
<223> n = A,T,C or G

```

```

<400> 292
gaaaaataa tcogtttaat tgaaaaacot gnaggatact attccactcc cccanatgag 60
gaggctgagg anaccaaacc cctacatcac ctctgtagcca cttctgatac tcttcacgag 120
gcagcaggca aagacaatcc ccaaaacctc nacaaaagca attccaaggg ctgctgcagc 180
taccaccanc acatttttcc tcagccagcc cccaatcttc tccacacagc cctccttatg 240
gatcgcttcc tcgttgaaat taatcccaca gccocagta acattaatgc ancaggagtc 300
ggggactcgg ttcttcgaca tggaagggat tttctcccaa tctgtgtagt tagcagcccc 360
acagcactta a                                     371

```

```

<210> 293
<211> 361
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 75, 196, 222
<223> n = A,T,C or G

```

```

<400> 293
gatttaaaag aaaacacttt attgttcagc aattaaaagt tagccaaata tgtatttttc 60
tcataatttt attngatgt tatcaacatc aagtaaaatg ctcatcttca tcatttgctt 120
ctgttcatgt ttctttgaac acgtcttcaa ttttcttccc aaaatgctgc atgccacact 180
tgaggtaacg aagcanaagt atttttaaac atgacagcta anaacattca tctacagcaa 240
cctatatgct caatacatgc cgcgtgatcc tagtagtttt ttcaaacctc tctacaagtt 300
tttgaaaaac atctgttatg atgactttca tacaccttca cctcaaaggc tttcttgccc 360
c                                     361

```

```

<210> 294
<211> 391
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 26, 77, 96, 150, 203, 252, 254, 264, 276
<223> n = A,T,C or G

```

```

<400> 294
tatttttaag tttaattatg attcanaaaa aatcgagcga ataactttct ctgaaaaaat 60
atattgactc tgtatanacc acagttattg gggganaagg gctggtaggt taaattatcc 120
tattttttat tctgaaaatg atattaatan aaagtcccggt ttccagtcgt attataaaga 180
tacatatgcc caaaatggct ganaataaat acaacaggaa atgcaaaagc tgtaaagcta 240
agggcatgca ananaaaatc tcanaataacc caaagnggca acaaggaaag ttgggctgga 300

```

```

atttgaagtt atttcagtca tctttgtctt tggctccatg tttcaggatg cgtgtgaact 360
cgatgtaatt gaaattccccc tttttatcaa t 391

```

```

<210> 295
<211> 343
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 145, 174, 205, 232
<223> n = A,T,C or G

```

```

<400> 295
ttcttttgtt ttattgataa cagaaactgt gcataattac agatttgatg aggaatctgc 60
aaataataaa gaatgtgtct actgccagca aaatacaatt attccatgcc ctctcaacat 120
acaatatatg agttcttcac accanatggc tctggtgtaa caaagccatt ttanatgttt 180
aattgtgctt ctacaaaacc ttcanagcat gaggtagtgt cttttaccta cnatatttct 240
cacattttcca ttattacact tttagtggag taaaatcctt ttaacatagc ctgcggatga 300
tctttocaaa aagccaagcc tcatattcaa agggtttatt tct 343

```

```

<210> 296
<211> 241
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 96, 98, 106, 185
<223> n = A,T,C or G

```

```

<400> 296
ttcttggata ttggtgtgtt ttgtgaaaa gttttgttt ttcttctcag tcaactgaat 60
tattttctcta ctttgccttc ctgatgccca catgananaa cttaanataa ttcttaacag 120
cttcacattt ggaaaaaaa aaaacctggt ttctcatggy aaacccagga gttgaaagt 180
gatanatgcg tctcaaaatc taaggctctg ttcagcttta cattatgtta ctgacggtt 240
t 241

```

```

<210> 297
<211> 391
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 12, 130
<223> n = A,T,C or G

```

```

<400> 297
gttgtggctg anaatgctgy agatgctcag ttctctccct cacaaggtag gccacaaatt 60
cttgttggtg ccctcacatc tggggtcttc aggcaccagc catgctctgc gaggagtgt 120
gtcaggacan accatgtccg tgctaggccc aggcacagcc caacctctcc tcatccaagt 180
ctctccaggg ttctgtgtcc cgatgggcaa ggatgacccc tccagtggct ggtacccacc 240
catcccacta cccctcacat gctctcactc tccatcaggt ccccaatcct ggcttccctc 300
ttcacggaact ctcaaagaaa aggaaggata aaacctaaat aaaccagaca gaagcagctc 360
tggaaaagta caaaaagaca gccagggtg t 391

```

```

<210> 298

```

<211> 321
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 14, 30, 76, 116, 201, 288, 301
 <223> n = A,T,C or G

```
<400> 298
caagccaaac tgtntccagc tttattaaan atactttcca taaacaatca tggattttca 60
ggcaggacat gggcanacaa tcgttaacag tatacaacaa ctttcaaatc ccttnttca 120
atggactacc aaaaatcaaa aagccactat aaaacccaat gaagtcttca tctgatgctc 180
tgaacaggga aagtttaag ngagggtga catttcacat ttatgcattt gtttaacaac 240
ttttcacaag cgcacctga ctttcaggaa gtgaaatgaa aatggcnaaa tttatctgaa 300
natccacaat ctaaaaatgg a                                     321
```

<210> 299
 <211> 401
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 104, 268, 347
 <223> n = A,T,C or G

```
<400> 299
tatcataaag agtgttgaag tttatttatt atagcaccat tgagacattt tgaaatttga 60
attggtataaa aaataaaaaa aaaagcattt gaattgtatt tggnggaaca gcaaaaaaag 120
agaagtatca tttttcttgg tcaaattata ctgtttccaa acatttttga aataaataac 180
tgggaattttg tcggtcactt gcactgggtg acaagattag aacaagagga acacatatgg 240
agttaaatatt tttttgttgg gatttcanat agagtttggt ttataaaaaa caaacagggc 300
caacgtccac accaaattct tgatcaggac caccaatgtc atagggngca atatctacaa 360
taggtagtct cacagccttg cgtgttcgat attcaaagac t                                     401
```

<210> 300
 <211> 188
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 48
 <223> n = A,T,C or G

```
<400> 300
tgaatgcttt gtcattattaa gaaagttaaa gtgcaataat gtttgaanac aataagtggc 60
gggttatctt gtttcttaata agataaaact ttttgccttt gctttatctt attagggagt 120
tgtatgtcag tgtataaaac atactgtgtg gtataacagc cttaataaat tcttttaaaag 180
gaaaaaaaaa                                     188
```

<210> 301
 <211> 291
 <212> DNA
 <213> Homo sapiens

<400> 301

```

aagattttgt tttattttat tatggctaga aagacactgt tatagccaaa atcggaatg 60
acactaaaga aatcctctgt gcttttcaat atgcaaatat atttcttcca agagttgcc 120
tggtgtgact tcaagagttc atgttaactt cttttctgga aacttctttt tcttagttgt 180
tgtattcttg aagagcctgg gccatgaaga gcttgccctaa gttttggcca gtgaacctct 240
tgatgttctg gcagtaagtg tttatctggc ctgcaatgag cagcaggtcc a 291

```

```

<210> 302
<211> 341
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 25
<223> n = A,T,C or G

```

```

<400> 302
tgatttttca taatttttatt aaatnatcac tgggaaaact aatggttcgc gtatcacaca 60
attacactaac aatctgatag gagtggtaaa accagccaat ggaatccagg taaagtacaa 120
aaacgccacc ttttattgtc ctgtcttatt tctcgggaag gagggttcta ctttacacat 180
ttcatgagcc agcagtggac ttgagtaca atgtgtaggt tccttgtggt tatagctgca 240
gaagaagcca tcaaatctct gaggacttga catctctcgg aaagaagcaa actagtggat 300
ccccgggct gcaggaattc gatatcaagc ttatcgatac c 341

```

```

<210> 303
<211> 361
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 15, 27, 92, 124, 127, 183, 198, 244, 320
<223> n = A,T,C or G

```

```

<400> 303
tgacagacgt aaatnaattt tatttngnnt cacagaacat actaggcgat ctogacagtc 60
gtccgtgtac agcccaccaa cccccaaccc tntacctcgc agccacccta aaggcgactt 120
caanaanatg gaaggatctc acggatctca ttccataatg tccgcggaag tctcacacag 180
tanacagacg gagttganat gctggaggat gcagtcacct cctaaactta cgaccaccca 240
ccanacttca tcccagccgg gacgtctctc cccacccgag tcttccccat ttcttctctt 300
actttgcgcg agttccaggn gtctctgttc caccagtccc acaaagctca ataaatacca 360
a 361

```

```

<210> 304
<211> 301
<212> DNA
<213> Homo sapiens

```

```

<220>
<221> misc_feature
<222> 23, 104, 192
<223> n = A,T,C or G

```

```

<400> 304
ctctttacaa cagcctttat ttncggccct tgatcctgct cggatgctgg tggaggccct 60
tagctccgcc cgccaggctc tgtgcgcgct cccgcaggc gcanattcat gaacacgggt 120
ctcaggggct tgaggccgta ctccccagc gggagctggt cctccagggg ctccccctcg 180
aaggtcagcc anaacaggtc gtctctgcaca cctccagcc cgctcacttg ctgcttcagg 240

```

tgggccacagg tctcgctcag ccgcacctcg taggtgtctgc tgcggccctt gttattctctc 300
a 301

<210> 305
<211> 331
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> 3, 36, 60, 193, 223
<223> n = A,T,C or G

<400> 305
ganaggctag taacatcagt tttattgggt tgggngggca accatagcct ggctgggggn 60
ggggctggcc ctcacagggt gttgagttcc agcagggtct ggtccaaggt ctgggtgaatc 120
tcgacgttct cctccttggc actggccaag gtctcttcta ggtcatcgat gggtttctcc 180
aactttgcc aacacctctc ggcaaacctct gctcgggtct canctcctt cagctctctcc 240
tccaacaggt tgatctctc ttcataatta tcttctttgg gggaatactc ctctctctgag 300
gccatcaggg acttgagggc ctggtccatg g 331

<210> 306
<211> 457
<212> DNA
<213> Homo sapiens

<400> 306
aatatgtaaa ggtaataact tttattatat taaagacaat gcaaacgaaa aacagaattg 60
agcagtgcaa aatttaaagg actgttttgt tctcaaaagt gcaagtttca aagccaaaag 120
aatttatatgt atcaaatata taagtaaaaa aaagttagac ttccaagcct gtaatcccaag 180
cacttttgga ggctgaggca ggtggatcac taacattaaa aagacaacat tagattttgt 240
cgatttatag caattttata aatatataac ttgtcactt ggatcctgaa gcaaaaaaat 300
aaagtgaatt tgggattttt gtacttggtt aaaaagttaa cacctctaat tcacaactag 360
tggatccccc gggctgcagg aattcgatat caagcttctc gataccgtcg acctcgaggg 420
ggggcccggt acccaattcg ccttatagtg agtcgta 457

<210> 307
<211> 491
<212> DNA
<213> Homo sapiens

<400> 307
gtgcttgagc ggaaccgggc gctcgttccc caccocggcc ggcgcgccat agccagccct 60
ccgtcaacct ttcaacgcac cctcggactg ccccaaggcc ccgcgccgcg ctccagcgcc 120
gcgcagccac gcgcgccgcg gccgcctctc cttagtcgc gccatgaaga ccgcgtccac 180
ctcgacggtg cgcacagaact accaccagga ctccagggcc gccatcaaac gccagatcaa 240
cctggagctc taacgctcct acgtttaact gtccatgtct tactactttg acccgcatga 300
tgtggccttg aagaactttg ccaataactt tcttcaccaa tctcatgagg agagggaaca 360
tgctgagaaa ctgatgaagc tgcagaacca acgaggtggc cgaatcttc ttcaggatata 420
caagaaacca gactgtgatg actgggagag cgggctgaat gcaatggagt gtgcattata 480
tttgaaaaaa a 491

<210> 308
<211> 421
<212> DNA
<213> Homo sapiens

<400> 308

```

ctcagcgctt cttctttctt ggtttgatcc tgactgetgt catggcggtc cctctggaga 60
aggccctgga tgtgatgggt tcacacctcc acaagtactc gggcaaaagag ggtgacaagt 120
tcaagctcaa caagtcagaa ctaaaggagc tgcctgacccg ggagctgcccc agctctcttg 180
ggaaaaggac agatgaagct gctttccaga agctgatgag caacttggac agcaacaggg 240
acaacagagt ggaactccaa gagtactgtg tcttctgttc ctgcactgcc atgatgtgta 300
acgaattctt tgaaggcttc ccagataagc agcccaggaa gaaatgaaa ctcctctgat 360
gtggttgggg cgtctgccag ctggggccct cctgtgcgcc agtgggcaat tttttttt 420
c 421

```

<210> 309

<211> 321

<212> DNA

<213> Homo sapiens

<400> 309

```

accaaatggc ggtgacgcc ggtgcagcgg gggggcccg gggccctggt gggccctggga 60
tgggaaacgc cggtggcttc cgcggaggtt tcggcagttg catccggggc cggggtcgcg 120
gccgtggacg gggccggggc cgaggcccg ggcctcgcg agctcgcgg aggcgaaggc gaggataagg 180
agtggatgcc cgtcaccaag ttgggcccgt tggccaagga catgaagatc aagtcctctg 240
aggagatcta tctctttctc ctgccattta aggaatcaga gatcattgat ttcttctctg 300
gggcctctct caaggatgag g 321

```

<210> 310

<211> 381

<212> DNA

<213> Homo sapiens

<400> 310

```

ttaaccagcc atattggctc aataaatagc ttccgtaagg agttaatttc cttctagaaa 60
tcaagtccta tttttctctg aaactcaatt ttaaatagtc caattccatc tgaagccaag 120
ctgtgtctcat tttcattcgg tgacattctc tcccatgaca ccagaaggcg gcagaagaac 180
cacatttttc atttatagat gtttgcatcc tttgtattaa aattattttg aaggggttgc 240
ctcattggat ggcttttttt tttttctctc agggagaaag ggagaaatgt acctggaaat 300
taatgtatgt ttacattctc ttgcaaatcc ctgtacatag agatatattt ttaaatgctg 360
aatgtaacaa catactgtga a 381

```

<210> 311

<211> 538

<212> DNA

<213> Homo sapiens

<400> 311

```

tttgaattta caccaagaac ttctcaataa aagaaaatca tgaatgctcc acaatttcaa 60
cataccacaa gagaagttta tttcttaaca ttgtgttcta tgattatttg taagaccctc 120
accaagttct gatatctttt aaagacatag ttcaaaattg cttttgaaaa tctgtattct 180
tgaataatcc ctgtgtgtgt attaggtttt taaataccag ctaaaaggatt acctcaactg 240
gtcatcagta cctctcattt cagctcccca agatgatgtg tttttgctta ccctaagaga 300
ggttttcttc ttatttttag ataattcaag tgcttagata aattatgttt tctttaagt 360
tttatggtaa actcttttaa agaaaattta atatgttata gctgaatctt ttgggtaact 420
ttaaactctt atcatagact ctgtacatat gttcaaatta gctgcttgcc tgatgtgtgt 480
atcatcggtg ggtgacaga acaaacatat ttatgatcat gaataatgtg ctttgtaa 538

```

<210> 312

<211> 176

<212> DNA

<213> Homo sapiens

<400> 312

```

ggaggagcag ctgagagata gggtcagtga atgcggttca gcctgtacc tctctgtct 60
tcatagaacc attgccttag aattattgta tgacacgttt tttgttggtt aagctgtaag 120
gttttgttct ttgtgaacat ggggtatttg aggggagggg ggaggaggta gggaa 176

```

```

<210> 313
<211> 396
<212> DNA
<213> Homo sapiens

```

```

<400> 313
ccagcaacccc caggccctgg gggacctggg ttctcagaact gccaaagaag ccttgccatc 60
tggcgctccc atggctcttg caacatctcc ccttcgtttt tgagggggtc atgcgggggg 120
agccaccagc cctcactctg gttcggagga gagtgcaggaa gggccaagca cgacaaagca 180
gaaacatcgg atttggggaa cgcgtgtcaa tccttgtgct gcaggggctg ggcggggagag 240
actgttctgt tccttgtgta actgtgttgc tgaagacta cctcgttctt gtcttgatgt 300
gtcaccgggg caactgcctg ggggcgggga tgggggcagg gtggaagcgg ctccccattt 360
tataccaaag gtgtacatc tatgtgatgg gtgggg 396

```

```

<210> 314
<211> 311
<212> DNA
<213> Homo sapiens

```

```

<400> 314
cctcaacatc ctcagagagg actggaagcc agtccttacc ataaactcca taatttatgg 60
cctgcagtat ctctctcttg agcccaaccc cgaggaccca ctgaacaagg aggccgcaga 120
ggctctgcag aacaaccggc ggcgtgttga gcagaacgtg cagcgtcca tgcggggtgg 180
ctacatcgcc tcacactact ttgagcgctg cctgaaatag ggttggcgca taccaccccc 240
cgccacggcc caaagccctg gcatcccctg caaatattta ttggggccca tgggtagggg 300
tttggggggc g 311

```

```

<210> 315
<211> 336
<212> DNA
<213> Homo sapiens

```

```

<400> 315
tttagaacat gtttatcatc caagactact ctaccctgca acattgaaact cccaagagca 60
aatccacatt cctcttgagt tctgcagctt ctgtgtaaat agggcagctg tcgtctatgc 120
cgtagaacat catgatctga ggaccattca tggaaagctg taaatagctt agtcctgggga 180
gtcttcata aagttttgca tggagcaaac aaacaggatt aaactgattt tgggtccctc 240
agccctctaa aagcataggg cttagcctgc aggtctcctt gggctttctc tgtgtgtgta 300
gtttgtgaaa cactatagca tctgttaaga tccagt 336

```

```

<210> 316
<211> 436
<212> DNA
<213> Homo sapiens

```

```

<400> 316
aacatggctc gcgtgcctta agagagacgc ttccctgcaga acaggacctg actacaaaga 60
atgtttccat tggaaattgt ggtaaagact tggagtttac aatctatgat gatgatgatg 120
tgtctccatt cctggaaggt cttgaagaaa gaccacagag aaaggcacag cctgctcaac 180
ctgctgatga acctgcagaa aaggctgatg aaccaatgga acattaagtg ataagccagt 240
ctatatatgt attatcaaat atgtaagaat acaggaccca catactgatg acaataatct 300
atacttgtga ccaaaagttg cagagtgtgt gaatgctatg ttttaggaat cagtcocagat 360
gtgagttttt tocaagcaac ctcaactgaa cctatataat ggaatacat tttctttgaa 420
agggtctgta taatca 436

```


<210> 317
 <211> 196
 <212> DNA
 <213> Homo sapiens

<400> 317
 tattctctgt gaagatgata tactatTTTT gTtaagcgtg tctgtattta tgtgtgagga 60
 gctgctggct tgcagtcgcg gtgcacgtgg agagctggtg cccggagatt ggacggcctg 120
 atgctccctc ccctgcctcg gtccaggga gctggccgag ggtcctggct cctgaggggc 180
 atctgcacct ccccca 196

<210> 318
 <211> 381
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 8, 9, 102, 122, 167, 182, 193, 235, 253, 265, 266, 290, 321, 378
 <223> n = A,T,C or G

<400> 318
 gacgcttng ccgtaacgat gatcgagac atcctgctgt tcgggagctt gctgatgaat 60
 gcggggcgg tgctgaactt taagctgaaa aagaaggaca cncagggctt tggggagggag 120
 tncaggggag ccaacacagg tgacaacatc cgggaattct tgcTgancct cagatacttt 180
 cnaatcttca tencctgtg gaacatcttc atgatgttct gcatgatgtg gctgntcggc 240
 tcttgaatcc cancgatgaa accannaact cactttcccg ggatgccgan tctccattcc 300
 tccattctct atgactcaa naatgttttt gacaaaaaa cgcacaacct tcccagaag 360
 tccaagctcg tggTggngg a 381

<210> 319
 <211> 506
 <212> DNA
 <213> Homo sapiens

<400> 319
 ctaagcttta cgaatggggT gacaacttat gataaaaact agagctagtg aattagccta 60
 ttgttaaata cctttgttat aattgatagg atacatcttg gacatggaat tgttaagcca 120
 cctctgagca gtgtatgtca ggacttgttc attaggttgg cagcagaggg gcagaaggaa 180
 ttatacaggt agagatgtat gcagatgtgt ccatatatgt ccatatttac attttgatag 240
 ccattgatgt atgcattctc tggctgtact ataagaacac attaatccaa tggaaataca 300
 ctttgttaat attttaatgg tatagatctg ctaatgaatt ctcttaaaaa cactactgtat 360
 tctgtttctg tgtgtttcat tttaaattga gcattaaggg aatgcagcat ttaaatcaga 420
 actctgccaa tgcttttata tagaggcgtg ttgcattttt tgtcttatat gaaatttctg 480
 tcccaagaaa ggcaggatta catott 506

<210> 320
 <211> 351
 <212> DNA
 <213> Homo sapiens

<400> 320
 ctgacctgca ggacgaaacc atgaagagcc tgatccttct tgccatctct gccgccttag 60
 cggtagttaac tttgtgttat gaatcacatg aaagcatgga atcttatgaa cttaatccct 120
 tcattacaag gagaatgca aataccttca tatccctcca gcagagatgg agagctaag 180
 tccaaagagag gatccgagaa cgctctaagc ctgtccacga gctcaatagg gaagcctgtg 240

atgactacag actttgcgaa cgctacgcc a tggtttatgg atacaatgct gcctataatc 300
gctacttcag gaagcgccga gggaccaaat gagactgagg gaagaaaaaa a 351

<210> 321

<211> 421

<212> DNA

<213> Homo sapiens

<400> 321

ctgggagcgc ttccagctgct tcaagatgaa gctgaacatc tccttccag ccaactggctg 60
ccagaaactc attgaagtgg acgatgaacg caaacttcgt actttctatg agaagcgat 120
ggccacagaa gttgctgctg acgctctggg tgaagaatgg aaggggtatg tgggtccgaat 180
cagtggtggg aacgacaaac aaggtttccc catgaagcag ggtgtcttga cccatggccg 240
tgtccgcctg ctactgagta aggggcattc ctgttacaga ccaaggagaa ctggagaaa 300
aaagagaaaa tcagttcgtg gttgcattgt ggatgcaaat ctgagcgctc tcaacttgg 360
tatgttaaaa aaaggagaga aggatattcc tggactgact gatactacag tgccctcgccg 420
c 421

<210> 322

<211> 521

<212> DNA

<213> Homo sapiens

<400> 322

agcagctctc ctgccacagc tctccacccc ctgaaaatgt tcgcctgctc caagtttgc 60
tcaactccct ccttggctcaa gagcaactca cagctgctga gccgtccgct atctgcagtg 120
gtgctgaaac gaccggagat actgacagat gagagcctca gcagcttggc agtctcatgt 180
cccttacctc cacttgtctc tagccgcagc ttccaaacca gcgccattc aagggacatc 240
gacacagcag ccaagttcat tggagctggg gctgccacag ttgggtctggg ttggtctggg 300
gctgggattg gaaotgtgtt tgggagcctc atcattgggt atgcccagaa ccttctctg 360
aagcaacagc tcttctctca cgcattctg ggctttgcc tctcgaggc cagtgggctc 420
ttttgtctga tggtagcctt tctcatctc ttgtccatgt gaaggagcgc tctccacctc 480
ccatagtctc cccgcgtctg gttggccccc tgtgttctt t 521

<210> 323

<211> 435

<212> DNA

<213> Homo sapiens

<400> 323

ccgaggtgag acgcgtgaga cttctccgcc gcagacgcgc ccgcgatgag ctacgtgcc 60
tctactctgc tgggtgccct agggggcaac tctcccccgc gcgccaaaga catcaagaag 120
atcttggaac cgtgggtat cgaggcgagc gacgaacggc tcaacaagg tctcagtgag 180
ctgaatggaa aaaacattga agcgtcatt gccacaggta ttggcagct tggcagtgta 240
cctgctgggt gggctgtagc cgtctctgct gccacaggct ctgcagccc ctgctctggt 300
ctgcccctgc ctgcagcaga ggagaagaaa gatgagaaga aggaggagtc tgaagagtc 360
gatgatgaca tgggatttgg cctttttgat taaattcctg ctccccgca aataaagcct 420
ttttacacat ctcaa 435

<210> 324

<211> 521

<212> DNA

<213> Homo sapiens

<400> 324

aggagatgca ctttcgtgac ccgcaagacc agggctggaa cgcogagatc acgtgcaga 60
tgggtcagta caagaatcgt caggccatcc tggcggtcaa atccacggcg cagaagcagc 120
agcacttggt ccagcagcag cccccctcgc agccgcagcc gcagccgagc ctccagcccc 180

```

aaccgccagcc tcagccctcag ccgcaacccc agcccccaatc acaaccccag cctcagcccc 240
aaccacaagcc tcagcccccag cagctccacc cgtatccgca tccacatcca catccacaet 300
ctcatctccca ctccgaccca caccctccacc cgcacccgca tccgcaccaa ataccgcacc 360
cacacccaca gccgcactcg cagccgcacg ggcaccggct tctccgcagc acctccaact 420
ctgctctgaaa ggggcagctc ccgggcaaga caagggtttg aggacttgag gaagtgaggac 480
gagcacattt ctattgtctt cacttggtac aaaagcaaaa c 521

```

<210> 325

<211> 451

<212> DNA

<213> Homo sapiens

<400> 325

```

attttctattt coattaacct ggaagctttc atgaatatcc tcttctttta aaacatttta 60
acattatttta aacagaaaaa gatgggctct tcttggttag ttgtttacatg atagcagaga 120
tatttttact tagattactt tgggaatgag agattgtttg ctgtaactct ggcactgtac 180
agtgaatgtg tctgtagttg tgttagtttg cattaagcat gtataacatt caagtatgtc 240
atccaaataa gaggcatata cattgaattg tttttaatcc tctgacaagt tgactcttcg 300
accccccccc ccacccaaga cattttaata gtaaatagag agagagagaa gagttaatga 360
acatgagtya gtgttccact ggccaggatga cttttcaata gctcaaatca atttcagctg 420
ctttatcact tgaattatta acttaatttg a 451

```

<210> 326

<211> 421

<212> DNA

<213> Homo sapiens

<220>

<221> misc_feature

<222> 296

<223> n = A,T,C or G

<400> 326

```

cgcggtcgta agggctgagg atttttggtc cgcacgctcc tgctctgtac tcacgcgtgt 60
tcgctctcgc cgaggaacaa gtcggtcagg aagccccgcg gcaacagcca tggcttttaa 120
ggataccgga aaaacacccg tggagccgga ggtggcaatt caccgaattc gaatcacctt 180
aacaagccgc aacgtaaaat ccttggaata ggtgtgtgct gacttgataa gaggcgcaaa 240
agaaaagaat ctcaaaagtga aaggaccagt tcgaatgcct accaagactt tgagantcac 300
tacaagaaaa actccttgtg gtgaaggttc taagacgtgg gatcgtttcc agatgagaat 360
tcacaagcga ctcatgtact tgcacagtc tctctgagatt gttaagcaga ttacttccat 420
c 421

```

<210> 327

<211> 456

<212> DNA

<213> Homo sapiens

<400> 327

```

atcttgacga ggctgcgggtg tctgtgtgcta ttctccgagc ttccgaatgc cgccaaagga 60
cgacaagaag aagaaggagc ctggaaaatc ggccaagaaa gacaaagacc cagtgaacaa 120
atccgggggg aaggccaaaaa agaagaagtg gtccaaaggc aaagtctggg acaagctcaa 180
taacttagtc ttgtttgaca aagctacctc tgataaactc tgtaaggaga ttcccaacta 240
taaaactata accccagctg ttgtctctga gagactgaag attcaggact ccctggccag 300
ggcagccctt cgagcctccc ttagtaaaag acttatcaaa ctgggtttcaa agcacagagc 360
tcaagttaatt tacaccagaa ataccaaggg tggagatgct ccagctgctg gtgaagatgc 420
atgaatagggt ccaaccagct gtacatttgg aaaaaat 456

```

<210> 328

<211> 471
 <212> DNA
 <213> Homo sapiens

<400> 328
 gtggaagtga catcgtcttt aaacccctgcg tggcaatccc tgacgcaccc ccgtagtgcc 60
 caggggaagac agggcgaccc ggaagtccaa ctacttcctt aagatcatcc aactattgga 120
 tgattatccg aaatgtttca ttgtgggagc agacaatgtg ggctccaagc agatgcagca 180
 gatccgcatg tcccttcgcg ggaaggctgt ggtgctgatg ggcaagaaca ccatgatgcy 240
 caaggccatc cgagggcgacc tggaaaacaa ccagctctg gagaaactgc tgccctcata 300
 ccgggggaat gtgggctttg tgttcaccaa ggaggacctc actgagatca ggacatgtt 360
 gctggccaat aaggtgccag ctgctgcccg tgcctggtgc attgcccat gtgaagtcc 420
 tgtgccagcc cagaacactg gtctcgggcc cgagaagacc tctttttcc a 471

<210> 329
 <211> 278
 <212> DNA
 <213> Homo sapiens

<220>
 <221> misc_feature
 <222> 154, 204
 <223> n = A,T,C or G

<400> 329
 gtttaaacctt aagcttggtta ccgagctcgg atccactagt ccagtggtgt ggaattctag 60
 aaattgagat gcccccacag gccagcaaat gttccttttt gtccaaagtc tatttttatt 120
 ccttgatatt ttcttttttt tttttttttt ttgnggatgg ggaactgtga atttttctaa 180
 aggtgctatt taacatggga gganagcgtg tgcggctcca gccagcccg ctgctcactt 240
 tccaccctct ctccacctgc ctctggcttc tcaggcct 278

<210> 330
 <211> 338
 <212> DNA
 <213> Homo sapiens

<400> 330
 ctcaggtctc aacatcgaat acgcccaggg ccccttcgcg ctattcttca tagccgaata 60
 cacaacattt attataataa acaccctcacc cactacaatc ttcttaggaa caacatagta 120
 cgcatccttc cctgaactct acacaacata ttttgtcacc aagaccctac ttctaaacct 180
 cctgttctta tgaattcgaa cagcatacc cagattccgc taacgaacct tcataacct 240
 cctatgaaaa aacttcctac cactcaccct agcattactt atatgatag tctccatacc 300
 cctacaatc tccagcattc cccctcaaac ctataaaaa 338

<210> 331
 <211> 2820
 <212> DNA
 <213> Homo sapiens

<400> 331
 tggcaaaatc ctggagccag aagaaaggac agcagcattg atcaatctta cagctaaccat 60
 gttgtacctg gaaaacaatg ccagactca atttagtgag ccacagtaca cgaacctggg 120
 gctcctgaac agcatggacc agcagattcg gaacggctcc tcgtccacca gtcccataaa 180
 cacagacacc gcgcagaaca gctgcacggc gccctcgccc tacgcacagc ccagcccccac 240
 ctctgatctc ctctctccat caccgcgcat cccctccaac accgactacc caggcccgca 300
 cagttccgag gttgtccttc agcagtcgag caccgccaag tcggccacct ggaagttatc 360
 cactgaactg aagaaactct actgcctaat tgcataagca tgcacctc agatacaagt 420
 gatgaccaca cctctcagg gagctgttat ccggcccatg cctgtctaca aaaaagctga 480

gcacgtcacg	gaggtggtga	agcgggtgcc	caaccatgag	ctgagccgtg	agttcaacga	540
gggaacagatt	gccctcctta	gtcatttgat	tcgagtagag	gggaacagcc	atgccacgta	600
tgtagaagat	cccatccacg	gaagacagag	tgtgtctggt	ctctatgagc	cacccacagt	660
tggcactgaa	ttaacgacag	ctctgtacaa	tctcatgttg	aacagcagtt	gtgttgagg	720
gatgaacgga	cgctcoattt	taatcattgt	tactctggaa	accagagatg	ggcaagtctt	780
gggcccgcgc	tgctttgagg	cccggaatctg	tgcttgccca	ggaagagaca	ggaaggcgga	840
tgaagatagc	atcagaaagc	agcaagtttc	ggacagatca	agaacgggtg	atggtacgaa	900
ggcccgcgtt	cgtcagaaca	cacatggtat	ccagatgaca	tccatcaaga	aacgaagatc	960
ccagatgatg	gaactgttat	acttaccagt	gagggggcgt	gagacttatg	aaatgctgtt	1020
gaagatcaaa	gagtcctctg	aactcatgca	gtaccttctc	cagcacacaa	tgaacaagta	1080
caggcaaacg	caacagcagc	agcaccagca	cttacttcag	aaacagacct	caatacagtc	1140
tccatctcca	tatgtaaca	gctccccacc	cttgaacaaa	atgaacagca	tgaacaagct	1200
gccttctctg	agccagetta	tcaaacctca	gcagcgcaac	gccctcactc	ctacaacocat	1260
tcttgatggc	atgggagcca	acattcccat	gatgggcacc	cacatgccaa	tggtctggaga	1320
catgaatgga	ctcagcccca	cccaggcact	ccctccccc	ctctccatgc	catccacctc	1380
ccactgcaca	ccccacactc	cgtatccac	agattgcagc	attgtcagtt	tcttgacgag	1440
gttggtgctg	tcatcatgtc	tggactattt	cacgaccag	gggctgacca	ccatctatca	1500
gattgagcat	tactccatg	atgatctggc	aagtctga	atccctgagc	aatttcgaca	1560
tgcatctcgg	aagggcatcc	tggaccaccg	gcagctccac	gaattctctc	ccoctttctca	1620
tctctcggcg	accocaaagca	gtgcctctac	agtcagtgtg	ggctccagtg	agaccggggg	1680
tgagcgtggt	attgatgctg	tgcgattcac	ccctcggcag	accatctctt	ccccaccocg	1740
agatgagtg	aatgacttca	actttgacat	ggatgctcgc	cgcaataagc	aacagcgcat	1800
caaaagagag	ggggagtgag	cctcacccatg	tgagctcttc	ctatccctct	cctaactgcc	1860
agccccctaa	aagcaactcct	gcttaattctt	caaagccttc	tccctagctc	ctcccccttc	1920
tcttctctga	tcttcttagg	gaaggagaa	taagaggcta	ctctttacct	aacatctgac	1980
ctggcatctca	attcttgatt	tggccttaag	ccttcaaaac	tatagcttgc	agaactctgag	2040
ctggcatggc	taggtgtgaag	tgagcaaaaa	agagttgggt	gtctccttaa	gctgcagaga	2100
ttctctactg	acttttataa	agcatgttca	cccttatagt	ctaagactat	atatataaat	2160
gtataaatat	acagttataga	tttttgggtg	gggggcattg	agttatttgt	aaatgtaat	2220
ttaaatgaaa	gaaaattgag	tgtcaccttat	tgaccatttt	ttaatttact	tgtttttggat	2280
gggtgtgtca	tactcctctc	cttaaggggg	atcatgtatg	gtgataggta	tctagagcgt	2340
aatgctacat	gtgagtgcca	tgtatgtacag	attctttcag	ttctttggat	tctaaataca	2400
tgccacatca	aacctttgag	tagatccatt	tccattgctt	attatgtagg	taagactgta	2460
gatatgtatt	ctttttctcag	tgtttggtata	ttttatatta	ctgacatttc	ttctatgtagt	2520
gatggttccac	gtttgggtga	tttaatccag	ttataagaag	aagtctcatg	ccaaacggctg	2580
ctcttttagtt	tttgggttgg	aatgaggaaa	attcttaaaa	ggcccatagc	gctggacttca	2640
aaaaaccocg	agctcatgta	tttgagcata	tcagtaaccc	ccttaaatat	aataccacaga	2700
taccttatct	tacaattgtg	attgggaaaa	catttgtctg	cttaacaga	ggtattaaaa	2760
ctaaatttca	ctactagatt	gactaactca	ataacacatt	tgctactggt	gtaagaattc	2820

<210> 332

<211> 2270

<212> DNA

<213> Homo sapiens

<400> 332

tcgttgatata	caaaagacagt	tgaaggaaat	gaattttgaa	acttcacggt	gtgccacct	60
acagctatgc	ctgcaccctt	acatccagcg	tttcgtagaa	accagctca	tttctcttgg	120
aaagaagatt	attacagcat	caccatgtcc	cagagcacac	agacaaatga	attctcagtt	180
ccagaggttt	tcacagatata	ctgggatttt	ctggaacagc	ctatatgttc	agttcagcco	240
atttgattgta	acttttggga	tgaacacatca	gaagatggtg	cgacaaacaa	gattgagatt	300
agcatggact	gtatccgatc	gcaggactcg	gacctgagtg	accocatgtg	gccacagcta	360
acggaacctgg	ggctctggaa	cagcatggac	cagcagattc	agaacgggtc	ctcgtccaac	420
agtcocctata	acacagacaa	cgcgcgaaac	agcgtcacgg	cgccctcgcc	ctaogcacag	480
ccagctccca	ctctcgatgc	tctctctcca	tcacccgcc	tcccctccaa	cacogactac	540
ccaggccocg	acagtttctg	cgtgtccttc	cagcagtcga	gcacggccaa	gtcgggccac	600
tggagctgatt	ccactgaact	gaagaaactc	tactgcaaaa	ttgcaaaagc	atgccccatc	660

cagatcaagg	tgatgacccc	acctcctcag	ggagctgtta	tccgcgccat	gctgtgtctac	720
aaaaaagctg	agcagctcac	ggaggtgggtg	aagcgggtgcc	ccaaccatga	gctgagccgt	780
gaattcaacg	agggaacagat	tgccctctct	agtcatttga	ttcagtaga	ggggaacagc	840
catggccag	atgtagaaga	tccatcacaca	ggaagacaga	gtgtgctggt	accttatgag	900
ccaccgccag	ttggcaactga	attcacgaca	gtcttgtaca	atttcattgtg	taacagcagt	960
tgtgttgagg	ggatgaacccg	ccgtccaatt	ttaatcattg	ttactctgga	aaccagagat	1020
gggcaagtcc	tgggccgacg	ctgctttgag	gccggatct	gtgcttgccc	aggaagagac	1080
aggaaggcgg	atgaagatag	catcagaaga	cagcaagttt	cggacagtag	aaagaacggt	1140
gatgtatcga	agcgcccggt	tcgtcagaac	acacatggtta	tcagatgac	atccatcaag	1200
aaacgaagat	ccccagatga	tgaactgttta	tacttaccag	tgagggggccg	tgagacttat	1260
gaaatgctgt	tgaagatcaa	agagtcctcg	gaactcatgc	agtaaccttc	tcagcacaca	1320
attgaaacgt	acaggcaaca	gcaacagcag	cagcaccagc	acttacttca	gaaacagacc	1380
caaatcagat	ctccatcttc	atatggtaac	agctccccc	ctctgaacaa	aatgaacagc	1440
atgaacaagc	tgccttctgt	gagccagctt	atcaaccctc	agcagcgcaa	cgccctcact	1500
ctctacaacca	ttcctgatgg	catgggagcc	aacattccca	tgatgggac	ccacatcca	1560
cctctggagg	acatgaatgg	actcagcccc	accagggcac	tcctctcccc	actctccatg	1620
ccatccacct	cccatcgac	acccccacct	ccgtatccaa	cagattgcag	cattgtcggt	1680
ttcttagcga	ggttggtgtg	ttcatcatgt	ctggactatt	tcacgaccca	ggggctgacc	1740
acccttatct	agatttagaca	ttactccatg	gatgatctgg	caagtctgaa	aatccctgag	1800
caattctcgac	atgcgatctg	gaaggggcatc	ctggacgtcca	ggcagctcca	cgaaattctcc	1860
tccccttctc	atctcctgct	gaccccaagc	agtgcctcta	cagtcagtagt	gggtccagct	1920
gagccccggg	gtgagcgtgt	tattgatgct	gtgcgattca	ccctcgcgca	gaccatctct	1980
ttcccccacc	gagatgagtg	gaatgaactc	aactttgaca	tgtgatgctg	cgcaataaag	2040
caacagcgca	tcaaaagaga	gggggagtg	gcctcaacct	gtgagctctt	ccatctccctc	2100
ttctaaactg	cagcccccta	aaagcaactc	tgcttaatct	tcaaaagcctt	ctccctgact	2160
ctcccccttc	ctcttctgtc	atttcttagg	ggaaggagaa	gtaagagcgt	acctcttacc	2220
taacatctga	ctgggcattct	aattctgatt	ctggcttttaa	gccttcaaaa		2270

<210> 333

<211> 2816

<212> DNA

<213> Homo sapiens

<400> 333

tcgttgatct	caaagacagt	tgaaggaaat	gaattttgaa	acttcacggt	gtgccacct	60
acagtagtat	ctcgaccctt	acatccagcg	tttcgtagaa	accagctca	ttctcttctg	120
aaagaaagtt	attaccgatc	caccatgtcc	cagagcacac	agacaaatga	attctcagat	180
ccagaggttt	tcacagatat	ctgggatttt	ctggaacagc	ctatatgttc	agttcacgcc	240
attgacttga	acttttgtga	tgaaccatca	gaagatgggt	cgacaaacaa	gattgagatt	300
agcatggact	gtatccgcag	gcaggaactgc	gaacttgagt	accctatgtg	gccacagtag	360
acgaaacctg	ggctctctgaa	cagcatggac	cagcagattc	agaaagcgtc	ctctgcacc	420
atgcctctata	acacagacca	cgcgagaaac	agcgtcacgg	cgccctcgcc	ctacgcaacg	480
ccagctctcca	ctctctgacg	tcctctccca	tcaccgcgca	tcctctccaa	accagactac	540
ccaggcccg	acagtttoga	cgtgtccttc	cagcagtcga	gcaccgcgca	gtcggccacc	600
tgagctgatt	ccactgaact	gaagaaactc	tactgcgaaa	ttgcgaaagc	atgccccatc	660
cagatcaagg	tgatgacccc	acctcctcag	ggagctgtta	tccgcgccat	gctgtctctc	720
aaaaaagctg	agcagctcac	ggaggtgggtg	aagcgggtgcc	ccaaccatga	gctgagccgt	780
gaattcaacg	agggaacagat	tgccctctct	agtcatttga	ttcagtaga	ggggaacagc	840
catgccccag	atgtagaaga	tccatcacaca	ggaagacaga	gtgtgctggt	accttatgag	900
ccaccgccag	ttggcaactga	attcacgaca	gtcttgtaca	atttcattgtg	taacagcagt	960
tgtgttgagg	ggatgaacccg	ccgtccaatt	ttaatcattg	ttactctgga	aaccagagat	1020
gggcaagtcc	tgggccgacg	ctgctttgag	gccggatct	gtgcttgccc	aggaagagac	1080
aggaaggcgg	atgaagatag	catcagaaga	cagcaagttt	cggacagtag	aaagaacggt	1140
gatgtatcga	agcgcccggt	tcgtcagaac	acacatggtta	tcagatgac	atccatcaag	1200
aaacgaagat	ccccagatga	tgaactgttta	tacttaccag	tgagggggccg	tgagacttat	1260
gaaatgctgt	tgaagatcaa	agagtcctcg	gaactcatgc	agtaaccttc	tcagcacaca	1320
attgaaacgt	acaggcaaca	gcaacagcag	cagcaccagc	acttacttca	gaaacatctc	1380
ctttcagcct	gcttcaggaa	tgagctgtgtg	gagcccgga	gagaaactcc	aaaaaatct	1440

gacgtcttct	ttagacattc	caagccccc	aaccgatcag	tgtaccata	gagccctatc	1500
tctatatttt	aagtgtgtgt	gttgatttct	catgtgtata	tgtgagtggt	tgtgtgtgta	1560
tgtgtgtggt	tgtgtatcta	gccctcataa	acaggacttg	aagacacttt	ggctcagaga	1620
cccaactgtg	caaaggcaca	aagccactag	tgagagaaac	ttttgaaggg	actcaaacct	1680
ttacaagaaa	ggatgttttc	tgacgatttt	gtatccttag	acoggccatt	tgaggggtgag	1740
gaaccoactgt	gtttgtctgt	gagctttctg	ttgttttctg	ggagggaggg	gtcaggtggg	1800
gaagggggga	taagatgttt	tattggaacc	cttttctgtc	ttcttctgtt	gtttttctaa	1860
aattcacagag	gaagcttttg	acgaggtctc	aaacttaaga	tgtcttttta	agaaaaggag	1920
aaaaaagtgt	tattgtctgt	tgcataaagta	agttgtaggt	gactgagaga	ctcagtcaga	1980
cccttttaatt	ctgtggtcatg	taataatatt	gcaagtagta	agaaacgagg	gtgtcagagt	2040
tactgtctggg	cagcagagtg	atcattacca	aaagtaatca	actttgtggg	tgagagagttc	2100
tttgtgagaa	cttgcatatat	tttgtctctc	ccctcatgtg	taggtagaac	atttcttaat	2160
gctgtgtacc	tgccctgtcc	actgtatgtt	ggcatctgtt	atgctaaagt	ttttcttgta	2220
catgaacccc	tggaagacct	actacaaaaa	aactgttgtt	tgccccctat	agacagtgaa	2280
ctcattttgt	gcttttaata	gaagacaaaa	tcacccccag	taatatgtcc	cttacgtagt	2340
ttgttaccat	tattcaaaag	tcaaaataga	atttgaagcc	ctctacaaaa	attctgtatt	2400
aatttgccta	attagagctt	ctatccctca	agcctaccta	ccataaaacc	agccataatta	2460
ctgagtgtgt	tcagtgcatt	tagccaggag	acttacgttt	tgagtgaagt	gactccaagc	2520
agacgttgta	aaatcagcac	tctgtgactg	gaattataag	attgaaaggg	tagactactt	2580
ttcttttttt	tactcaaaag	tttagagaat	ctctgtttct	ttccatttta	aaacactatt	2640
ttaaagtaat	agcataaaga	ctttaaaat	gttctctccc	tccatctctc	cacaccagat	2700
accagcagct	gtatttttct	tcaccaagac	aatgatttct	tgttatttag	gctgttgcct	2760
ttgtggatgt	gtgattttta	ttttcaataa	acttttgcat	cttggtttta	aagaaa	2816

<210> 334
 <211> 2082
 <212> DNA
 <213> Homo sapiens

<400> 334						
agatgtatca	gcgactgcac	accaggtctg	tatgatacag	cctattgtct	ccgggtgcga	60
aaactgtcca	gcattgtgat	tggtgggata	ctgaattgaa	taaccgaatac	tgtaggcaat	120
tgtaacacag	tggttaagtct	ttgtgtatct	aaacatagct	aaacacacaaa	aggtatagta	180
agaattatgtt	attataatct	tatggaaacta	tcattgtata	tgtggtttgt	caaccagaatc	240
gtagtatact	agcacaggac	ttgtgcttatg	atgtgccaag	cacagctctc	agtactaaat	300
ccattaatct	tcataatcaac	cctaggaggt	aaacttcttaa	gtagattcat	atttgaaggg	360
tctcgggggt	gggggggttg	caaaatcctg	gagccagaag	aaaggacagc	agcatttgatc	420
aatcttttgt	ctaacattgtt	gtacctggaa	aacaatgccc	agactcaatt	tattgtgacca	480
cagtcacaga	acctggggct	cctgaacagc	atggaccagc	agattcagaa	cggtcctctg	540
tcocaccagct	ccataaacac	agaccaagcg	cagaacagcg	tcacggcgcc	ctcgccctac	600
gcacagccca	gctccacctt	cgatgctctc	tctccatcac	ccgccatccc	ctccaacacc	660
gactaccagc	gcgccagcac	tttcgaagtg	tccttccagc	agtcagagac	cgccaagtgt	720
gcocactgga	gcatctccag	tgaaactgaag	aaactctact	gccaaattgc	aaagacatgc	780
cccatccaga	tcagggtgat	gacccacact	cctcagggag	ctgttatccg	cgccaatgct	840
gtctacacaaa	aagctgagca	cgtaacggag	gtggtgaagc	gtggtgccc	ccatgagctg	900
agcgtggaat	tcacagagtg	acagattgac	cctcctagtc	atttgattgc	agtagagggg	960
aaacgcctat	ccagtagtgt	agaagatccc	atcacaggaa	gacagagtg	gctgttacct	1020
tatgagccac	ccaggttgat	cactgaattc	acgacagctc	tgtaacaatt	catgtgttaac	1080
acaggttgtg	ttggagggat	gaacggcggt	ccaattttta	tcattgtgta	cttggaacac	1140
agagatgggc	aagtctctggg	ccgacgctgc	tttgaggccc	ggatctgtgc	ttgcccaggga	1200
agagacagga	agggcgatga	agatagcatc	agaaagcagc	aagttttcga	cagtcacatcc	1260
aaactgtgat	gtacgaagcg	ccgctctcgt	cagaacacac	attggtatga	gatgacatgc	1320
atcaagaaac	gaagatccccc	agatgatgaa	ctgtttatact	taccagttag	ggggcgtgag	1380
acttatgaaa	tgctgttgaa	gatcaaaag	tccttcgagta	tccttcgagta	ccttccctac	1440
cacacaattg	aaacgtacag	gcaacagcaa	cagcagcagc	accagcactt	acttcagaaa	1500
cagtgagtggt	atcaacgtgt	catttttagga	ggcattgag	ccggtgactt	tatttggatc	1560
agcaataggg	tgatttgatga	gcaatgtgga	acataatggg	agatagcaga	ttgtcataga	1620
ttcagatgac	ctggtatgac	aaccctcttt	cagttgcaac	cttttttacg	tgtcttatta	1680

taaccttccc	ttcagaattc	cacttatgtt	ctgaaattaa	atcacaaacca	ttttctggtga	1740
attacaaga	aactccact	aacagttctc	ttctctatat	gcctgggtcca	tacacactaa	1800
cagtaagatc	acaactctatt	tggtagtgat	gtgtatattt	gaaacacatga	aatctttttc	1860
catcccaatt	gattgtctta	taaatctcct	gggatgcaca	ctatccactt	ttgggaataa	1920
cactgtagac	cagggtatgc	aaaataggctt	tactataata	taaatgtgact	tgtttgaatg	1980
ctgtaatgag	aaagattctg	agacactagt	catgataatt	ggggaaatat	ctgggtgcag	2040
aaggataaag	tagcatcatg	ttgcctgatt	ttagcatctc	tg		2082

<210> 335

<211> 4849

<212> DNA

<213> Homo sapiens

<400> 335

cgttgatata	aaagacagtt	gaaggaaatg	aattttgaaa	cttcacgggtg	tgccacccta	60
cagtaactgcc	ctgaccctta	catccagcgt	ttcgtagaaa	cccacgctca	tttctcttgg	120
aaagaaagttt	ttaccagatc	caccatgtcc	cagagcacac	agacaaatga	attcctcagt	180
ccagagagttt	tcacagatat	ctgggatttt	ctggaaacagc	ctatatgttc	agttcacgcc	240
attgacttga	actttgtgga	tgaacatcca	gaagatggtg	cgacaaacaa	gattgagatt	300
agcatggact	gtatccgatc	gcaggactcg	gacctgagtg	accccatgtg	gccacagtac	360
acgaacactgg	ggctctcgaa	cagcatggac	cagcagattc	agaaaggctc	ctcgtccacc	420
agtcctcata	acacagacaa	cgcgcagaac	agcgtccagg	cgccctcgcc	ctaocgaacg	480
cccagctcca	ccttcgatgc	tctctctcca	tcaccoccca	tcccctccaa	caccgactac	540
ccaggccocg	acagttttga	cgtgtccttc	cagcagtoga	gcacgcgcaa	gtcgggcacc	600
tggaagctatt	ccactgaact	gaagaaactc	tactgccaaa	ttgcacagac	atgcccctac	660
cagatccaag	tgatgacccc	acctcctcag	ggagctgtta	tcgcgcacat	gcctgtctac	720
aaaaaagctg	agcacgtcac	ggaggttggtg	aagcggtgcc	ccaacatgat	gctgagccgt	780
gaattccaag	agggacagat	tgccctcctc	agtcatttga	ttcgagttaga	ggggaacagc	840
ctgccccagt	attgtagaaga	tcccatcaca	ggaagacaga	gtgtgctggt	acottatgag	900
ccaccccgag	ttggcaactga	attcacagaca	gtcttgtaca	atttcatgtg	taacagcagt	960
tggttttgag	gtgtgaacgc	ccgtccaatt	ttaatcattg	ttactctgga	aaccagagatt	1020
gggcaagtcg	tgggccgaag	ctgctttgag	gcccggatct	gtgcttgccc	aggaagagac	1080
aggaaggcgg	atgaagatag	catcagaaga	cagcaagttt	cggacagtag	aaagaacggg	1140
gatggtaaga	agcgcocgtt	togtcagaac	acacatggta	tcacagatga	atccatcaag	1200
aaacgaagat	cccagatga	tgaactgtta	tacttaccag	tgagggggcg	tgagacttat	1260
gaaatgctgt	tgaagatcaa	agagtcctcg	gaactcatgc	agtaaccttc	tacgacacaa	1320
attgaaacgt	acaggcaaca	gcaacagcag	cagcaccagc	acttactcca	gaacagagac	1380
toaatcacgt	ctccatcttc	atatggtaac	agctccccc	ctctgaacaa	aattgaacagc	1440
attgaacaaac	tgccctctgt	gagcgaagctt	atcaaacctc	agcagcgcaa	cgccctcaat	1500
cctacaacgc	tctcgatagg	catggggagcc	aaacttcccc	tgatgggcac	ccaatgcaca	1560
atggctggag	acatgaatgg	actcagcccc	accagggcac	tccttcccc	actctccatg	1620
ccatccacct	ccagatgcac	acccccacct	cogtatcccc	cagatttgag	catgttcagt	1680
ttcttagoga	ggttgggctg	ttcatcatgt	ctggactatt	tcaagaccca	ggggctgacc	1740
acacatctgc	attcttgagca	ttactccatg	gatgatctgg	caagctgtga	aatccctgag	1800
caatttgcag	attcgcatctg	gaagggcata	ctggaacacc	ggcagctcca	cgaattctcc	1860
tcocctcttc	attcctcgcg	gaccccaagc	agtgccctta	cagtcatgtg	gggctccaat	1920
gagacccggg	gtgagcgctg	tattgatgtc	gtgcgattca	cctccgcgca	gaccatctct	1980
ttccaccccc	gagatgagtg	gaatgacttc	aaacttgaca	tggaatgctc	cgcgaataag	2040
caacagcgca	tcaaagagga	gggggagtg	gcctcaccat	gtgagctctt	cctatccctc	2100
tcctaaactgc	cagcycccta	aaagcactcc	tgcttaatot	tcaaaagcct	ctccctagct	2160
ctctccctct	ctcttgtctg	atttcttagg	ggaaggagaa	gtaaggaggt	acctcttacc	2220
taacatctga	ctcggcatct	aattctgatt	ctggctttaa	gccttcaaaa	ctatagcttg	2280
cagaactgta	gctgcacatg	ctaggttagaa	gtgagcaaaa	aagagttggg	tgctctccta	2340
agctcgagag	attcttcatt	gacttttata	aagcatgttc	acctcttacc	ctcaagcata	2400
tatatataaa	tgtataaata	tacagtatag	atttttgggt	ggggggcatt	gagtatgtgt	2460
taaaatgtaa	tttaaatgaa	agaaaattga	gttgacatta	ttgacatttt	tttaatttac	2520
ttgttttggg	tggttgtctc	atactccttc	ccttaagggg	tatcatgtat	ggtgataggt	2580
atctagagct	taatgtaca	tgtgagtgac	gatgatgtac	agattctttc	agttcttttg	2640

attctaaaata	catgccacat	caaacctttg	agtagatcca	tttccattgc	ttattatgta	2700
ggtaagacgt	tagatatgta	ttctttttct	agtgttggtg	tattttatatt	tactgacatt	2760
tcttctagtg	atgatgggtc	acgttggggg	gattttaatcc	agttataaga	agaagttcoat	2820
gtccaaaacgt	ccctcttagt	ttttggttgg	gaatgaggaa	aattctttaa	agggccatag	2880
cagcgagttc	aaaaaacacc	gacgtcatgt	atttgagcat	atacgaatacc	cccttaaat	2940
taataacaga	tacccttatct	tacaatatgt	atttgggaaa	caattgtgctg	cattacacagag	3000
gtattaaaac	taaaattcac	tactagattg	actaaactcaa	atacacatttt	gctcatgttg	3060
taagaattct	gattgatttg	attgggtaga	atgccatctca	tctagttcta	acagtgaggt	3120
tttactgtct	attaatatcc	agggtaaaata	ggaatcattc	agaaatgttg	agtcgtgact	3180
aaacagtaag	atatctcaat	gaaccataaa	ttcaactttg	taaaaaatctt	ttgaagcata	3240
gataatatgt	tttggtaaat	gtttcttttg	tttggtaaat	gtttctttta	aagaccctcc	3300
tattctataa	aactctgcat	gtagaggctt	gtttacottt	ctctctctaa	ggtttacaat	3360
aggagtggtg	atttgaaaaa	tataaaaatta	tgagattggt	tttctgtggg	catlaaattgc	3420
atcactgtat	ctattttctt	tttaaccoggt	aagagtttca	gtttgttgga	aagtaactgt	3480
gagaaccaga	tttccogtcc	atctccctta	gggactacc	atagacatga	aaggtcccca	3540
cagagcaaga	tcaatgctct	tcattggctgc	tggtgtctaa	accaactaaa	cgaagagttc	3600
ccttgaaact	ttgggaaaac	atgttaatga	caatattcca	gatctttcag	aaatataaca	3660
gatttttttg	catgcatgca	aatgagctct	gaaatctccc	catgcaatttc	ggctcaaggcg	3720
tgctattgca	caataagcttc	cattttaatt	ttaaagtga	aaaggggcag	cgtggtctca	3780
aaaggtaatg	tgtgttgctg	ctctgaaaag	tggtgtatata	ttttgttgga	aattgcatac	3840
tttgtatttt	gattattttt	ttttttctct	tggttagatg	ggatttccag	aaccacactt	3900
tgaacctttt	tttatcgctt	ttgtattttt	atgaaaaatac	cattttagtaa	gaataccaca	3960
taaaataaga	aaataatgcta	caatttttaag	aggggagggg	agggaaaagt	tttttttatt	4020
ttttttttta	aattttgtat	gttaaagaga	atgagtcctt	gatttcaaag	ttttgttgta	4080
cttaaatggt	aataagcact	gtaaactctt	gcaacaagca	tgacgctttg	caaacccatt	4140
aagggggaag	atgaaagctg	ttctctgttc	ctagtaagaa	gacaaactgc	ttcccttact	4200
ttgtcgaggg	tttgaataaa	octaggactt	ccgagctatg	tcagctatgt	caggttaaca	4260
ctagggcctt	gaaatattct	gtactgtgtc	tcattggatt	ggcaactagcc	aaagcagagg	4320
acccttctgt	gcttaactcc	tcattggcagc	ctactctcct	tgagtgtatg	agtagccaag	4380
gtaaggggta	aaaggatagt	aagcatagaa	accactagaa	agtgggctta	atggagtctt	4440
tgtggccctca	gctcaatgca	gttagctgaa	gaattgaaa	gtttttgttt	ggagacgttt	4500
ataaacagaa	atggaaaagca	gagttttcat	taaatccttt	tacotttttt	ttttcttgtt	4560
aatccctcaa	aataacagta	tgtgggatat	tgaattgtta	agggatattt	tttttctatt	4620
atttttataa	ttgtacaaaa	ttaaagcaat	gttaaaaagt	ttatattgct	tattaaattg	4680
ttcaaaaggt	attatcatatg	tgatcatatt	tttaagcttc	agttgtgtgt	cttctgggtac	4740
tttctgttat	gggcttttgg	ggagccagaa	gccaatctac	aatctctttt	tgtttggcag	4800
gacatgcaat	aaaattttaa	aaataaataa	aaactaatta	agaaataaa		4849

<210> 336

<211> 1386

<212> DNA

<213> Homo sapiens

<400> 336

atgttgtagc	tggaatacaa	tgcccagact	caatttagtg	agccacagta	cacgaacctg	60
gggctcctga	acagcatgga	ccagcagatt	cagaacggct	cctcgtccac	cagtcocctat	120
aaacacagac	acgcgcagaa	cagcgtcacg	ggcgcctcgc	cctacgcaca	gccacagcc	180
acctctcgtg	ctctctctcc	atcacccgcc	atccccctca	acacccagta	cccaggcccg	240
ccacagtctg	acgtgtcctt	ccagcagctg	agcaccgccca	agtccggcac	ctggacagtat	300
tcaactgaac	tgaagaacct	ctactgccaa	attgcaaaag	catgcccact	ccagatacaag	360
gtgatgcacc	accctctcca	gggagctggt	atcccgccca	tgccctgtcta	caaaaagact	420
ggagcagctc	cggaggtggg	gaagcggctg	cccaaccatg	agctgagccg	gaatttcaac	480
gagggacaga	ttgccctctc	tagtcaattg	attogagtag	aggggaacag	ccatgccccag	540
tatgtagaag	atcccatcac	aggaagacag	agtggtctgg	taccttatga	gccaccaccag	600
gttgccactg	aattcaagac	agtcctgtac	aatttcatgt	gtaacagcag	ttgtgttgga	660
gggatgaacc	gccgtccaat	tttaactcatt	gttactctgg	aaaccagaga	tgggcgaagt	720
ctggcccgac	gctgctttga	ggcccgagac	tgtgcttgcc	caggaagaga	cagggaaggcg	780
gatgaagata	gcattcagaaa	gcagcaaggt	tcggacagta	caaagaacgg	tgatgggtacg	840

```

aagcgcccggt   ttcgtcagaa   cacacatggt   atccagatga   catccatcaa   gaaacgaaga   900
tcccagcatgt   atgaactggt   atacttacca   gtgagggggc   gtgagactta   gtaaatgctg   960
ttgaagatcaa   aagagtcctt   ggaactcatg   cagtaccttc   ctacgacacac   aattgaaacg   1020
tacaggcaac   agcaaacagca   gcagcaccag   cacttacttc   agaaacagac   ctcaatacag   1080
ttcccatctt   catatggtaa   cagctcccca   cctctgaaca   aaatgaacag   catgaacaag   1140
ctgcctctgt   tgagccagct   tatcaacctc   cagcagcgca   acgcccctac   tctctacaac   1200
attctgtgat   gcctgggagc   caacattccc   atgatgggca   cccacatgac   aatggctgga   1260
gacatgaatg   gactcagccc   caccacggca   ctccctcccc   cactctccat   gccatccacc   1320
tcccactgca   cccccccacc   tccgtatccc   acagattgca   gcattgtcag   gatctggcaa   1380
gtctga

```

```

<210> 337
<211> 1551
<212> DNA
<213> Homo sapiens

```

```

<400> 337
atgtcccaga   gcacacagac   aaatgaattc   ctccagtcag   aggtttttcca   gcatatctgg   60
gattttctgg   aacagcctat   atgttcagtt   cagcccatgt   acttgaactt   tgttgatgaa   120
ccatcagaag   atgtgtcgag   aaacaagatt   gagattagca   tggactgtat   ccgatgcag   180
gaactcggacc   tgagtaccac   catgtggcca   cagtacacga   acctggggct   ctgaacagc   240
atggaccagc   agattccaaa   cggtctctcg   tccaccagtc   cctataaacac   agaacacgcy   300
cagaacacgcy   tcacggcgcc   ctccgctctc   gcacagccca   gctccacctt   cgatgctctc   360
ttctccatcac   ccgcatctcc   ctccaacacc   gactaccocag   gcccgacagc   ttctcgagtg   420
tccttcacag   agtcggagcac   cgccaagtgc   gccacctgga   cgtattccac   tgaactgaag   480
aaactctact   gccaaattgc   aaagacatgc   cccatccaga   tcaaggtgat   gaccccaact   540
ctccagggag   ctgtttatcc   cgccatgcct   gtctacaaaa   aaagctgagca   cgtcacggag   600
gtggtgaagc   ggtgccccaa   ccatgagctg   agccgtgaat   tcaacgaggg   acagattggc   660
ctctctagtc   atttgattcg   agtagagggg   aacagccatg   cccagtatgt   agaagatccc   720
atcacaggaa   gacagagtg   gctggtacct   tatgagccac   cccaggttgg   cactgaattc   780
acgcagctct   tgtacaattt   catgtgtaac   agcagttgtg   ttggagggat   gaaccccggt   840
ccaattttta   tcattgtttc   tctggaaccc   agagatgggc   aagtctctgg   ccgacgctgc   900
tttgaggccc   ggtatctgtc   ttgcccagga   agagacagga   aggcggatga   agatagcatc   960
agaagcagc   aagtttcgga   cagtacaag   aacggtgatg   gtacgaagcg   ccggttctgt   1020
cagaacacac   atggtatcca   gatgacatcc   atcaagaaac   gaagatcccc   agatgatgaa   1080
ctgttatact   taccagtgag   gggccgtgag   acttatgaaa   tgctgttgaa   gatcaaaag   1140
tccttgtaac   tcattgcagta   ccttctctcag   cacacaattg   aaacgtacag   gcaacagcaa   1200
cagcagcagc   accagcactt   acttcagaaa   cagacctcaa   tacagtctcc   atctctcatat   1260
ggtaacagct   cccacacctc   gaacaaaaatg   aacagcatga   acaagctgccc   ttctgtgagc   1320
cagcttatca   accctcagca   gcgcaacgoc   ctcaactcta   caacctctcc   tggatggcat   1380
ggagccaaca   ttcccatgat   gggcaccac   atgccaatgg   ctggagacat   gaatggactc   1440
agccccaccc   aggcactccc   tccccactc   tccatgccat   ccacctccca   ctgcacaccc   1500
ccactctcgt   atcccacaga   ttgcagcatt   gtcaggatct   ggcaagctgc   a

```

```

<210> 338
<211> 586
<212> PRT
<213> Homo sapiens

```

```

<400> 338
Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
1      5      10      15
Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Arg Asn
20     25     30
Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
35     40     45
Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Pro Thr Phe Asp Ala
50     55     60

```

Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Ser Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys
 450 455 460
 Ser Ser Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr
 465 470 475 480
 Gln Ile Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro
 485 490 495
 Glu Gln Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln
 500 505 510
 Leu His Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser
 515 520 525

Ala Ser Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val
 530 535 540
 Ile Asp Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro
 545 550 555
 Arg Asp Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn
 565 570 575
 Lys Gln Gln Arg Ile Lys Glu Glu Gly Glu
 580 585

<210> 339
 <211> 641
 <212> PRT
 <213> Homo sapiens

<400> 339
 Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1 5 10 15
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335

Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Gly
 500 505 510
 Phe Leu Ala Arg Leu Gly Cys Ser Ser Cys Leu Asp Tyr Phe Thr Thr
 515 520 525
 Gln Gly Leu Thr Thr Ile Tyr Gln Ile Glu His Tyr Ser Met Asp Asp
 530 535 540
 Leu Ala Ser Leu Lys Ile Pro Glu Gln Phe Arg His Ala Ile Trp Lys
 545 550 555 560
 Gly Ile Leu Asp His Arg Gln Leu His Glu Phe Ser Ser Pro Ser His
 565 570 575
 Leu Leu Arg Thr Pro Ser Ser Ala Ser Thr Val Ser Val Gly Ser Ser
 580 585 590
 Glu Thr Arg Gly Glu Arg Val Ile Asp Ala Val Arg Phe Thr Leu Arg
 595 600 605
 Gln Thr Ile Ser Phe Pro Pro Arg Asp Glu Trp Asn Asp Phe Asn Phe
 610 615 620
 Asp Met Asp Ala Arg Arg Asn Lys Gln Gln Arg Ile Lys Glu Glu Gly
 625 630 635 640
 Glu

<210> 340

<211> 448

<212> PRT

<213> Homo sapiens

<400> 340

Met Ser Gln Ser Thr Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1 5 10 15
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80

Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175
 Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185 190
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200 205
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215 220
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys His Leu Leu Ser Ala Cys
 405 410 415
 Phe Arg Asn Glu Leu Val Glu Pro Arg Arg Glu Thr Pro Lys Gln Ser
 420 425 430
 Asp Val Phe Phe Arg His Ser Lys Pro Pro Asn Arg Ser Val Tyr Pro
 435 440 445

<210> 341

<211> 356

<212> PRT

<213> Homo sapiens

<400> 341

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 1 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30

Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240
 Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Ser Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln
 355

<210> 342

<211> 680

<212> PRT

<213> Homo sapiens

<400> 342

Met Asn Phe Glu Thr Ser Arg Cys Ala Thr Leu Gln Tyr Cys Pro Asp
 1 5 10 15
 Pro Tyr Ile Gln Arg Phe Val Glu Thr Pro Ala His Phe Ser Trp Lys
 20 25 30
 Glu Ser Tyr Tyr Arg Ser Thr Met Ser Gln Ser Thr Gln Thr Asn Glu
 35 40 45
 Phe Leu Ser Pro Glu Val Phe Gln His Ile Trp Asp Phe Leu Glu Gln
 50 55 60

Pro Ile Cys Ser Val Gln Pro Ile Asp Leu Asn Phe Val Asp Glu Pro
 65 70 75 80
 Ser Glu Asp Gly Ala Thr Asn Lys Ile Glu Ile Ser Met Asp Cys Ile
 85 90 95
 Arg Met Gln Asp Ser Asp Leu Ser Asp Pro Met Trp Pro Gln Tyr Thr
 100 105 110
 Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn Gly Ser
 115 120 125
 Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser Val Thr
 130 135 140
 Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala Leu Ser
 145 150 155 160
 Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro His Ser
 165 170 175
 Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala Thr Trp
 180 185 190
 Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala Lys Thr
 195 200 205
 Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly Ala Val
 210 215 220
 Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr Glu Val
 225 230 235 240
 Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn Glu Gly
 245 250 255
 Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn Ser His
 260 265 270
 Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val Leu Val
 275 280 285
 Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val Leu Tyr
 290 295 300
 Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg Arg Pro
 305 310 315 320
 Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val Leu Gly
 325 330 335
 Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg Asp Arg
 340 345 350
 Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp Ser Thr
 355 360 365
 Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr His Gly
 370 375 380
 Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp Glu Leu
 385 390 395 400
 Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu Leu Lys
 405 410 415
 Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His Thr Ile
 420 425 430
 Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu Leu Gln
 435 440 445
 Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser Ser Pro
 450 455 460
 Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val Ser Gln
 465 470 475 480
 Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr Ile Pro
 485 490 495
 Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met Pro Met
 500 505 510
 Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro Pro Pro
 515 520 525

Leu Ser Met Pro Ser Thr Ser Gln Cys Thr Pro Pro Pro Tyr Pro
 530 535 540
 Thr Asp Cys Ser Ile Val Ser Phe Leu Ala Arg Leu Gly Cys Ser Ser
 545 550 555
 Cys Leu Asp Tyr Phe Thr Thr Gln Gly Leu Thr Thr Ile Tyr Gln Ile
 565 570 575
 Glu His Tyr Ser Met Asp Asp Leu Ala Ser Leu Lys Ile Pro Glu Gln
 580 585 590
 Phe Arg His Ala Ile Trp Lys Gly Ile Leu Asp His Arg Gln Leu His
 595 600 605
 Glu Phe Ser Ser Pro Ser His Leu Leu Arg Thr Pro Ser Ser Ala Ser
 610 615 620
 Thr Val Ser Val Gly Ser Ser Glu Thr Arg Gly Glu Arg Val Ile Asp
 625 630 635
 Ala Val Arg Phe Thr Leu Arg Gln Thr Ile Ser Phe Pro Pro Arg Asp
 645 650 655
 Glu Trp Asn Asp Phe Asn Phe Asp Met Asp Ala Arg Arg Asn Lys Gln
 660 665 670
 Gln Arg Ile Lys Glu Glu Gly Glu
 675 680

<210> 343

<211> 461

<212> PRT

<213> Homo sapiens

<400> 343

Met Leu Tyr Leu Glu Asn Asn Ala Gln Thr Gln Phe Ser Glu Pro Gln
 1 5 10 15
 Tyr Thr Asn Leu Gly Leu Leu Asn Ser Met Asp Gln Gln Ile Gln Asn
 20 25 30
 Gly Ser Ser Ser Thr Ser Pro Tyr Asn Thr Asp His Ala Gln Asn Ser
 35 40 45
 Val Thr Ala Pro Ser Pro Tyr Ala Gln Pro Ser Ser Thr Phe Asp Ala
 50 55 60
 Leu Ser Pro Ser Pro Ala Ile Pro Ser Asn Thr Asp Tyr Pro Gly Pro
 65 70 75 80
 His Ser Phe Asp Val Ser Phe Gln Gln Ser Ser Thr Ala Lys Ser Ala
 85 90 95
 Thr Trp Thr Tyr Ser Thr Glu Leu Lys Lys Leu Tyr Cys Gln Ile Ala
 100 105 110
 Lys Thr Cys Pro Ile Gln Ile Lys Val Met Thr Pro Pro Pro Gln Gly
 115 120 125
 Ala Val Ile Arg Ala Met Pro Val Tyr Lys Lys Ala Glu His Val Thr
 130 135 140
 Glu Val Val Lys Arg Cys Pro Asn His Glu Leu Ser Arg Glu Phe Asn
 145 150 155 160
 Glu Gly Gln Ile Ala Pro Pro Ser His Leu Ile Arg Val Glu Gly Asn
 165 170 175
 Ser His Ala Gln Tyr Val Glu Asp Pro Ile Thr Gly Arg Gln Ser Val
 180 185 190
 Leu Val Pro Tyr Glu Pro Pro Gln Val Gly Thr Glu Phe Thr Thr Val
 195 200 205
 Leu Tyr Asn Phe Met Cys Asn Ser Ser Cys Val Gly Gly Met Asn Arg
 210 215 220
 Arg Pro Ile Leu Ile Ile Val Thr Leu Glu Thr Arg Asp Gly Gln Val
 225 230 235 240

Leu Gly Arg Arg Cys Phe Glu Ala Arg Ile Cys Ala Cys Pro Gly Arg
 245 250 255
 Asp Arg Lys Ala Asp Glu Asp Ser Ile Arg Lys Gln Gln Val Ser Asp
 260 265 270
 Ser Thr Lys Asn Gly Asp Gly Thr Lys Arg Pro Phe Arg Gln Asn Thr
 275 280 285
 His Gly Ile Gln Met Thr Ser Ile Lys Lys Arg Arg Ser Pro Asp Asp
 290 295 300
 Glu Leu Leu Tyr Leu Pro Val Arg Gly Arg Glu Thr Tyr Glu Met Leu
 305 310 315 320
 Leu Lys Ile Lys Glu Ser Leu Glu Leu Met Gln Tyr Leu Pro Gln His
 325 330 335
 Thr Ile Glu Thr Tyr Arg Gln Gln Gln Gln Gln His Gln His Leu
 340 345 350
 Leu Gln Lys Gln Thr Ser Ile Gln Ser Pro Ser Ser Tyr Gly Asn Ser
 355 360 365
 Ser Pro Pro Leu Asn Lys Met Asn Ser Met Asn Lys Leu Pro Ser Val
 370 375 380
 Ser Gln Leu Ile Asn Pro Gln Gln Arg Asn Ala Leu Thr Pro Thr Thr
 385 390 395 400
 Ile Pro Asp Gly Met Gly Ala Asn Ile Pro Met Met Gly Thr His Met
 405 410 415
 Pro Met Ala Gly Asp Met Asn Gly Leu Ser Pro Thr Gln Ala Leu Pro
 420 425 430
 Pro Pro Leu Ser Met Pro Ser Thr Ser His Cys Thr Pro Pro Pro
 435 440 445
 Tyr Pro Thr Asp Cys Ser Ile Val Arg Ile Trp Gln Val
 450 455 460

<210> 344

<211> 516

<212> PRT

<213> Homo sapiens

<400> 344

Met Ser Gln Ser Thr 5 Gln Thr Asn Glu Phe Leu Ser Pro Glu Val Phe
 1 10 15
 Gln His Ile Trp Asp Phe Leu Glu Gln Pro Ile Cys Ser Val Gln Pro
 20 25 30
 Ile Asp Leu Asn Phe Val Asp Glu Pro Ser Glu Asp Gly Ala Thr Asn
 35 40 45
 Lys Ile Glu Ile Ser Met Asp Cys Ile Arg Met Gln Asp Ser Asp Leu
 50 55 60
 Ser Asp Pro Met Trp Pro Gln Tyr Thr Asn Leu Gly Leu Leu Asn Ser
 65 70 75 80
 Met Asp Gln Gln Ile Gln Asn Gly Ser Ser Ser Thr Ser Pro Tyr Asn
 85 90 95
 Thr Asp His Ala Gln Asn Ser Val Thr Ala Pro Ser Pro Tyr Ala Gln
 100 105 110
 Pro Ser Ser Thr Phe Asp Ala Leu Ser Pro Ser Pro Ala Ile Pro Ser
 115 120 125
 Asn Thr Asp Tyr Pro Gly Pro His Ser Phe Asp Val Ser Phe Gln Gln
 130 135 140
 Ser Ser Thr Ala Lys Ser Ala Thr Trp Thr Tyr Ser Thr Glu Leu Lys
 145 150 155 160
 Lys Leu Tyr Cys Gln Ile Ala Lys Thr Cys Pro Ile Gln Ile Lys Val
 165 170 175

Met Thr Pro Pro Pro Gln Gly Ala Val Ile Arg Ala Met Pro Val Tyr
 180 185
 Lys Lys Ala Glu His Val Thr Glu Val Val Lys Arg Cys Pro Asn His
 195 200
 Glu Leu Ser Arg Glu Phe Asn Glu Gly Gln Ile Ala Pro Pro Ser His
 210 215
 Leu Ile Arg Val Glu Gly Asn Ser His Ala Gln Tyr Val Glu Asp Pro
 225 230 235 240
 Ile Thr Gly Arg Gln Ser Val Leu Val Pro Tyr Glu Pro Pro Gln Val
 245 250 255
 Gly Thr Glu Phe Thr Thr Val Leu Tyr Asn Phe Met Cys Asn Ser Ser
 260 265 270
 Cys Val Gly Gly Met Asn Arg Arg Pro Ile Leu Ile Ile Val Thr Leu
 275 280 285
 Glu Thr Arg Asp Gly Gln Val Leu Gly Arg Arg Cys Phe Glu Ala Arg
 290 295 300
 Ile Cys Ala Cys Pro Gly Arg Asp Arg Lys Ala Asp Glu Asp Ser Ile
 305 310 315 320
 Arg Lys Gln Gln Val Ser Asp Ser Thr Lys Asn Gly Asp Gly Thr Lys
 325 330 335
 Arg Pro Phe Arg Gln Asn Thr His Gly Ile Gln Met Thr Ser Ile Lys
 340 345 350
 Lys Arg Arg Ser Pro Asp Asp Glu Leu Leu Tyr Leu Pro Val Arg Gly
 355 360 365
 Arg Glu Thr Tyr Glu Met Leu Leu Lys Ile Lys Glu Ser Leu Glu Leu
 370 375 380
 Met Gln Tyr Leu Pro Gln His Thr Ile Glu Thr Tyr Arg Gln Gln Gln
 385 390 395 400
 Gln Gln Gln His Gln His Leu Leu Gln Lys Gln Thr Ser Ile Gln Ser
 405 410 415
 Pro Ser Ser Tyr Gly Asn Ser Ser Pro Pro Leu Asn Lys Met Asn Ser
 420 425 430
 Met Asn Lys Leu Pro Ser Val Ser Gln Leu Ile Asn Pro Gln Gln Arg
 435 440 445
 Asn Ala Leu Thr Pro Thr Thr Ile Pro Asp Gly Met Gly Ala Asn Ile
 450 455 460
 Pro Met Met Gly Thr His Met Pro Met Ala Gly Asp Met Asn Gly Leu
 465 470 475 480
 Ser Pro Thr Gln Ala Leu Pro Pro Pro Leu Ser Met Pro Ser Thr Ser
 485 490 495
 His Cys Thr Pro Pro Pro Tyr Pro Thr Asp Cys Ser Ile Val Arg
 500 505 510
 Ile Trp Gln Val
 515

<210> 345

<211> 1800

<212> DNA

<213> Homo sapiens

<400> 345

gcgcctcatt gccactgcag tgactaaagc tgggaagacg ctggctcagtt cacotgcccc 60
 actggttggtt ttttaaacaa attctgatac aggcgacatc ctcaactgacc gagcaagat 120
 tgacattcgt atcatcactg tgcaccattg gcttctaggg actccagtgg ggtaggagaa 180
 ggaggtctga aacctcgca gagggatott gccctcatte tttgggtctg aaacactggc 240
 agtcgttgga aacaggactc agggataaac cagcgcaatg gattggggga cgcgtgcacac 300
 tttcatcggy ggtgtcaaca aacactccac cagcatcggy aagggttgga tcacagtcac 360

```

ctttattttc cgagtcgatg tctagtggt ggctgccag gaagtgtggg gtgacgagca 420
agaggacttc gtctgcgaaca cactgcaacc gggatgcaaa aatgtgtgct atgaccactt 480
ttttccgggtg tcccacatcc ggctgtgggg cctccagctg atcttctgct ccaccccagc 540
gctgctgggtg gccatgcctg tggcctacta caggcacgaa accactcgca agtttcggcg 600
aggagagaag aggaatgatt tcaaaagacat agaggacatt aaaaagccaca aggttcggat 660
agaggggtcgt ctgtgggtgga cgtacaccag cagcatcttt ttccgaatca tctttgaagc 720
agcctttatg tatgtgtttt acttccctta caatgggtac cactcgccct gggtgttgaa 780
atgtgggatt gaccocctgoc ccaacottgt tgactgcttt atttctaggc caacagagaa 840
gaccgtgtttt accatttttta tgatttctgc gtctgtgatt tgcatgtctg ttaacgtggc 900
agagttgtgc taccctctgc tgaaagtgtg ttttaggaga tcaaaagagag cacagacgca 960
aaaaaatcac cccaatcatg ccctaaaagg agttaagcag aatgaaatga atgagctgat 1020
ttcagatagt ggtcaaaatg caatcacagg tttcccaagc taaacatttc aaggtaaaat 1080
gtagctgcgt cataaggaga cttctgtctt ctccagaagg caataccaac ctgaaagttc 1140
cttctgtagc ctgaagagtt tgtaaatgac ttccataata aatagacact tgagttaaat 1200
ttttgtagga tacttgcctc attcatacac aacgtaaatca aatagtgggt ccactctctg 1260
aaacaagaga ctgcttgaca agggagcatt gcagtcactt tgacagggttc cttttaagtg 1320
gactctctga caaagtgggt actttctgaa aatttatata actgtgtgtg ataaggaa 1380
tttatccagg aattgatcac ttatttagga aaagatatatt ttataggctt ggatgttttt 1440
agttcccgact ttgaatttat ataaagtatt ttatataatg ctggctcttc ttacctggaa 1500
aaacatgoga tgttagtttt agaattacac cacaagtatc taaattttcca acttacaag 1560
ggtccctatct tgtaaatatt gttttgcatt gtctgttgcc aaatttgatg actgtcatga 1620
tacgcttaag gtgggaaagt gttcattgca caatatatt ttactgcttt ctgaatgtag 1680
acggaaacgt gtggaagcag aaggcttttt taactcatcc gtttggccga tcgttgagaa 1740
ccactgggag atgtggatgt ggttgccctc ttttgcctgt ccccggtgct taacctttct 1800

```

<210> 346

<211> 261

<212> PRT

<213> Homo sapiens

<400> 346

```

Met Asp Trp Gly Thr Leu His Thr Phe Ile Gly Gly Val Asn Lys His
1      5      10      15
Ser Thr Ser Ile Gly Lys Val Trp Ile Thr Val Ile Phe Ile Phe Arg
20     25     30
Val Met Ile Leu Val Val Ala Ala Gln Glu Val Trp Gly Asp Glu Gln
35     40     45
Glu Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
50     55     60
Tyr Asp His Phe Phe Pro Val Ser His Ile Arg Leu Trp Ala Leu Gln
65     70     75     80
Leu Ile Phe Val Ser Thr Pro Ala Leu Leu Val Ala Met His Val Ala
85     90     95
Tyr Tyr Arg His Glu Thr Thr Arg Lys Phe Arg Arg Gly Glu Lys Arg
100    105    110
Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys Lys His Lys Val Arg Ile
115    120    125
Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Ile
130    135    140
Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Phe Leu Tyr Asn Gly
145    150    155    160
Tyr His Leu Pro Trp Val Leu Lys Cys Gly Ile Asp Pro Cys Pro Asn
165    170    175
Leu Val Asp Cys Phe Ile Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
180    185    190
Ile Phe Met Ile Ser Ala Ser Val Ile Cys Met Leu Leu Asn Val Ala
195    200    205

```

Glu Leu Cys Tyr Leu Leu Lys Val Cys Phe Arg Arg Ser Lys Arg
 210 215 220
 Ala Gln Thr Gln Lys Asn His Pro Asn His Ala Leu Lys Glu Ser Lys
 225 230 235 240
 Gln Asn Glu Met Asn Glu Leu Ile Ser Asp Ser Gly Gln Asn Ala Ile
 245 250 255
 Thr Gly Phe Pro Ser
 260

<210> 347
 <211> 1740
 <212> DNA
 <213> Homo sapiens

<400> 347
 atgaacaac tgtatatcgg aaacctcagc gagaacgccg cccctcggga cctagaaagt 60
 atcttcaagg agcccaagat cccgggtgog ggaccccttc tggtagaagc ttgctacggc 120
 ttgcgtgact gcccgacga gagctgggcc ctcaaggcca tcgaggcgct ttcagggtaaa 180
 atagaactgc accgggaacc catagaagtt gagcaactcg tcccaaaaag gcaaaagatt 240
 cggaactctc agatacgaat tatcccgctc catttacagt gggagggtgt ggatagttaa 300
 ctagtccagt atggagtgtt ggagagctgt gagcaagtga acactgactc ggaactgca 360
 gtgttaaatg taactatttc cagtaaggac caagctagac aagcaactga caaactgaat 420
 ggatttcagt tagagaattt caccttgaaa gttagcctata tcctgtatga aacggccgcc 480
 cagcaaaacc ccttcagaca gccccgaggt cgcggggggc ttgggcagag gggctctcaa 540
 aggcagggtt ctccaggatc cgtatccaag cagaaaccat gtgatttgcc tctgcgctg 600
 ctgggttccca cccaatttgt tggagccatc ataggaaaag aaggtgccac cattcggaac 660
 atcaccaaac agaccagtc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720
 gagaagtgc tttactatct ctctactcct gaaggcactc ctgcggcttg taagtctatt 780
 ctggagatta tgcataagga agctcaagat ataaaattca cagaagagat ccccttgaag 840
 attttagctc ataataact tgttggacgt cttatttgga aagaaggag aaactctaaa 900
 aaaattgagc aagacacaga cactaaaatc acgatatctc cattgcagga attgacgctg 960
 tataatccag aacgcactat tacagttaaa ggcaatgttg agacatgtgc caaagctgag 1020
 gagggatcat taagaaaaat caggaggtct tatgaaaatg atattgcttc tatgaattct 1080
 caagcacatt taattctctg attaaatctg aacgccttgg gtctgttccc acccaactca 1140
 gggatgccac ctcccacctc agggcccccct tcagccatga ctctctccca cccgcagttt 1200
 gagcaatcag aaacggagac tgttcatctg tttatccag ctctatcagt cgggtgcctc 1260
 atcggcaagc agggccagca catcaagcag ctttctcgct ttgctggagc ttcaattaa 1320
 attgctccag cgggaagcac agatgtctaa gtgaggatgg tgattatcac tggaccacca 1380
 gaggtcaggt tcaaggctca gggaagaatt tatggaaaa ttaagaaga aaactttgtt 1440
 agtctctaaa aagaggtgaa acttgaagct catatcagag tgcactcctt tgcgtcggcg 1500
 agagtattgt gaagaaggag caaaacggtg aatgaacttc agaatttgtt aagtgcagaa 1560
 gttgttgttc cctgtgacca gacactgtgt gagaatgacc aagtggtgtt caaaataact 1620
 ggtcactctc atcgttgcca ggttgcacag agaaaaatc aggaatctct gactcaggt 1680
 aagcagcacc aacaacagaa ggctctgcaa agtggaccac ctgactcaag acggaagtaa 1740

<210> 348
 <211> 579
 <212> FRT
 <213> Homo sapiens

<400> 348
 Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
 1 5 10 15
 Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro
 20 25 30
 Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser

Trp	35				40				45						
	Ala	Leu	Lys	Ala	Ile	Glu	Ala	Leu	Ser	Gly	Lys	Ile	Glu	Leu	His
50						55					60				
Gly	Lys	Pro	Ile	Glu	Val	Glu	His	Ser	Val	Pro	Lys	Arg	Gln	Arg	Ile
65					70					75					80
Arg	Lys	Leu	Gln	Ile	Arg	Asn	Ile	Pro	Pro	His	Leu	Gln	Trp	Glu	Val
				85					90					95	
Leu	Asp	Ser	Leu	Leu	Val	Gln	Tyr	Gly	Val	Val	Glu	Ser	Cys	Glu	Gln
				100				105					110		
Val	Asn	Thr	Asp	Ser	Glu	Thr	Ala	Val	Val	Asn	Val	Thr	Tyr	Ser	Ser
				115			120					125			
Lys	Asp	Gln	Ala	Arg	Gln	Ala	Leu	Asp	Lys	Leu	Asn	Gly	Phe	Gln	Leu
						135						140			
Glu	Asn	Phe	Thr	Leu	Lys	Val	Ala	Tyr	Ile	Pro	Asp	Glu	Thr	Ala	Ala
145					150					155					160
Gln	Gln	Asn	Pro	Leu	Gln	Gln	Pro	Arg	Gly	Arg	Arg	Gly	Leu	Gly	Gln
				165					170					175	
Arg	Gly	Ser	Ser	Arg	Gln	Gly	Ser	Pro	Gly	Ser	Val	Ser	Lys	Gln	Lys
				180				185					190		
Pro	Cys	Asp	Leu	Pro	Leu	Arg	Leu	Leu	Val	Pro	Thr	Gln	Phe	Val	Gly
		195					200					205			
Ala	Ile	Ile	Gly	Lys	Glu	Gly	Ala	Thr	Ile	Arg	Asn	Ile	Thr	Lys	Gln
210						215						220			
Thr	Gln	Ser	Lys	Ile	Asp	Val	His	Arg	Lys	Glu	Asn	Ala	Gly	Ala	Ala
225					230					235				240	
Glu	Lys	Ser	Ile	Thr	Ile	Leu	Ser	Thr	Pro	Glu	Gly	Thr	Ser	Ala	Ala
				245					250					255	
Cys	Lys	Ser	Ile	Leu	Glu	Ile	Met	His	Lys	Glu	Ala	Gln	Asp	Ile	Lys
				260				265					270		
Phe	Thr	Glu	Glu	Ile	Pro	Leu	Lys	Ile	Leu	Ala	His	Asn	Asn	Phe	Val
				275				280				285			
Gly	Arg	Leu	Ile	Gly	Lys	Glu	Gly	Arg	Asn	Leu	Lys	Lys	Ile	Glu	Gln
290						295					300				
Asp	Thr	Asp	Thr	Lys	Ile	Thr	Ile	Ser	Pro	Leu	Gln	Glu	Leu	Thr	Leu
305					310					315				320	
Tyr	Asn	Pro	Glu	Arg	Thr	Ile	Thr	Val	Lys	Gly	Asn	Val	Glu	Thr	Cys
				325					330					335	
Ala	Lys	Ala	Glu	Glu	Glu	Ile	Met	Lys	Lys	Ile	Arg	Glu	Ser	Tyr	Glu
				340				345					350		
Asn	Asp	Ile	Ala	Ser	Met	Asn	Leu	Gln	Ala	His	Leu	Ile	Pro	Gly	Leu
				355			360					365			
Asn	Leu	Asn	Ala	Leu	Gly	Leu	Phe	Pro	Pro	Thr	Ser	Gly	Met	Pro	Pro
370						375					380				
Pro	Thr	Ser	Gly	Pro	Pro	Ser	Ala	Met	Thr	Pro	Pro	Tyr			

Leu	Gln	Asn	500	Leu	Ser	Ser	Ala	Glu	505	Val	Val	Val	Pro	Arg	510	Asp	Gln	Thr
Pro	Asp	Glu	515	Asn	Asp	Gln	Val	Val	520	Val	Lys	Ile	Thr	Gly	525	Gly	Phe	Tyr
Ala	Cys	Gln	530	Val	Ala	Gln	Arg	Lys	535	Ile	Gln	Glu	Ile	Leu	Thr	Gln	Val	540
545	Lys	Gln	His	Gln	Gln	550	Lys	Ala	Leu	Gln	Ser	Gly	Pro	Pro	Gln	555	Ser	560
Arg	Arg	Lys	565							570					575			

```
<210> 349
<211> 207
<212> DNA
<213> Homo sapiens
```

[illegible]

```
<210> 350
<211> 69
<212> PRT
<213> Homo sapiens
```

```

<400> 350
Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly
1      5      10      15
Ser Ser Gln Ile Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile
20      25      30
Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp
35      40      45
Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His
50      55      60
Gly Ala Asn Arg Phe
65

```

```
<210> 351
<211> 1012
<212> DNA
<213> Homo sapiens
```

[illegible]

```

gaggacttcg tctgcaaacac actgcaaccg ggaatgcaaaa atgtgtgcta tgaccacttt 660
ttcccggtgt cccacatccg gctgtgggccc ctcacgtgta tottcgtctc caccacagcg 720
ctgctgtggg ccatgcatgt ggcctactac aggcacgaaa ccactcgcaa gttagcgga 780
ggagagaaga ggaatgattt caaagacata gaggacatta aaaagcagaa ggttcggata 840
gaggggtgac tcgagcacca ccaccaccac cactgagatc cggctgctaa caaagccoga 900
aaggaaagctg agttggctgc tgccaccgct gagcaataac tagcataaac ccttgggggc 960
tctaaacggg tcttgagggg ttttttgcgt aaaggaggaa ctatatccgg at 1012

```

<210> 352

<211> 267

<212> PRT

<213> Homo sapiens

<400> 352

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
1      5      10      15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
20     25     30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
35     40     45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
50     55     60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
65     70     75
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
85     90     95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
100    105   110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
115    120   125
Leu Ala Glu Gly Pro Pro Ala Glu Phe Met Asp Trp Gly Thr Leu His
130    135   140
Thr Phe Ile Gly Gly Val Asn Lys His Ser Thr Ser Ile Gly Lys Val
145    150   155
Trp Ile Thr Val Ile Phe Ile Phe Arg Val Met Ile Leu Val Val Ala
165    170   175
Ala Gln Glu Val Trp Gly Asp Glu Gln Glu Asp Phe Val Cys Asn Thr
180    185   190
Leu Gln Pro Gly Cys Lys Asn Val Cys Tyr Asp His Phe Phe Pro Val
195    200   205
Ser His Ile Arg Leu Trp Ala Leu Gln Leu Ile Phe Val Ser Thr Pro
210    215   220
Ala Leu Leu Val Ala Met His Val Ala Tyr Tyr Arg His Glu Thr Thr
225    230   235
Arg Lys Phe Arg Arg Gly Glu Lys Arg Asn Asp Phe Lys Asp Ile Glu
245    250   255
Asp Ile Lys Lys Gln Lys Val Arg Ile Glu Gly
260    265

```

<210> 353

<211> 900

<212> DNA

<213> Homo sapiens

<400> 353

```

atgcatacacc atcaccatca caggcccgcg tccgataact tccagctgtc ccagggtggg 60
cagggtatcg ccattccgat cgggcaggcg atggcgatcg cgggccagat caagcttccc 120

```



```

accgttcata tcgggcctac cgccttcctc ggcttgggtg ttgtcgacaa caacggcaac 180
ggcgacacgag tccaacgcgt ggtcggggagc gctcggcgcg caagtctcgg catctccacc 240
ggcgacacgta tcaccgcggt cgacggcgct ccatcaact cgggccacgc gatggcggac 300
ggcgttaaac ggcatcatcc cggtagcgtc atctcggtag cctggcaaac caagtccggc 360
ggcacgcgta cagggaaacgt gacattggcc gagggacccc cggccgaatt ccacgaaacc 420
actcgcaagt tcaggcgagc agagaagagg aatgatttca aagacataga ggacattaaa 480
aagcagaagg ttcggataga ggggtcgctg tggtagcgt acaccagcag catcttttcc 540
cgaatcatct ttgaagcagc ctttatgtat gtgttttact tcttttaca tgggtaccac 600
ctgcctcggg tgttgaatg tgggattgac ccctgcccca acctgttga ctgctttatt 660
tctaggccaa cagagaagac cgtgtttacc atttttatga tttctgcgtc tgtgatttgc 720
atgctgctta acgtggccaga gttgtgctac ctgctgctga aagltgtgtt taggagatca 780
aagagagcac agacgcaaaa aaatcaccac aatcatgcc taaaggagag taagcagaat 840
gaaatgaatg agctgatttc agatagtggg caaatgcaa tcacaggttt cccaagctaa 900

```

<210> 354

<211> 299

<212> PRT

<213> Homo sapiens

<400> 354

```

Met His His His His His Thr Ala Ala Ser Asp Asn Phe Gln Leu
1      5      10      15
Ser Gln Gly Gly Gln Gly Phe Ala Ile Pro Ile Gly Gln Ala Met Ala
20     25     30
Ile Ala Gly Gln Ile Lys Leu Pro Thr Val His Ile Gly Pro Thr Ala
35     40     45
Phe Leu Gly Leu Gly Val Val Asp Asn Asn Gly Asn Gly Ala Arg Val
50     55     60
Gln Arg Val Val Gly Ser Ala Pro Ala Ala Ser Leu Gly Ile Ser Thr
65     70     75     80
Gly Asp Val Ile Thr Ala Val Asp Gly Ala Pro Ile Asn Ser Ala Thr
85     90     95
Ala Met Ala Asp Ala Leu Asn Gly His His Pro Gly Asp Val Ile Ser
100    105    110
Val Thr Trp Gln Thr Lys Ser Gly Gly Thr Arg Thr Gly Asn Val Thr
115    120    125
Leu Ala Glu Gly Pro Pro Ala Glu Phe His Glu Thr Thr Arg Lys Phe
130    135    140
Arg Arg Gly Glu Lys Arg Asn Asp Phe Lys Asp Ile Glu Asp Ile Lys
145    150    155    160
Lys Gln Lys Val Arg Ile Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser
165    170    175
Ser Ile Phe Phe Arg Ile Ile Phe Glu Ala Ala Phe Met Tyr Val Phe
180    185    190
Tyr Phe Leu Tyr Asn Gly Tyr His Leu Pro Trp Val Leu Lys Cys Gly
195    200    205
Ile Asp Pro Cys Pro Asn Leu Val Asp Cys Phe Ile Ser Arg Pro Thr
210    215    220
Glu Lys Thr Val Phe Thr Ile Phe Met Ile Ser Ala Ser Val Ile Cys
225    230    235    240
Met Leu Leu Asn Val Ala Glu Leu Cys Tyr Leu Leu Lys Val Cys
245    250    255
Phe Arg Arg Ser Lys Arg Ala Gln Thr Gln Lys Asn His Pro Asn His
260    265    270
Ala Leu Lys Glu Ser Lys Gln Asn Glu Met Asn Glu Leu Ile Ser Asp
275    280    285
Ser Gly Gln Asn Ala Ile Thr Gly Phe Pro Ser

```

290

<210> 355
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 355
 ggagtacagc ttcaagacaa tggg 24

<210> 356
 <211> 31
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 356
 ccatgggaat tcattataat aattttgttc c 31

<210> 357
 <211> 920
 <212> PRT
 <213> Homo sapiens

<400> 357
 Met Gln His His His His His Gly Val Gln Leu Gln Asp Asn Gly
 1 5 10 15
 Tyr Asn Gly Leu Leu Ile Ala Ile Asn Pro Gln Val Pro Glu Asn Gln
 20 25 30
 Asn Leu Ile Ser Asn Ile Lys Glu Met Ile Thr Glu Ala Ser Phe Tyr
 35 40 45
 Leu Phe Asn Ala Thr Lys Arg Arg Val Phe Phe Arg Asn Ile Lys Ile
 50 55 60
 Leu Ile Pro Ala Thr Trp Lys Ala Asn Asn Asn Ser Lys Ile Lys Gln
 65 70 75 80
 Glu Ser Tyr Glu Lys Ala Asn Val Ile Val Thr Asp Trp Tyr Gly Ala
 85 90 95
 His Gly Asp Asp Pro Tyr Thr Leu Gln Tyr Arg Gly Cys Gly Lys Glu
 100 105 110
 Gly Lys Tyr Ile His Phe Thr Pro Asn Phe Leu Leu Asn Asp Asn Leu
 115 120 125
 Thr Ala Gly Tyr Gly Ser Arg Gly Arg Val Phe Val His Glu Trp Ala
 130 135 140
 His Leu Arg Trp Gly Val Phe Asp Glu Tyr Asn Asn Asp Lys Pro Phe
 145 150 155 160
 Tyr Ile Asn Gly Gln Asn Gln Ile Lys Val Thr Arg Cys Ser Ser Asp
 165 170 175
 Ile Thr Gly Ile Phe Val Cys Glu Lys Gly Pro Cys Pro Gln Glu Asn
 180 185 190
 Cys Ile Ile Ser Lys Leu Phe Lys Glu Gly Cys Thr Phe Ile Tyr Asn
 195 200 205
 Ser Thr Gln Asn Ala Thr Ala Ser Ile Met Phe Met Gln Ser Leu Ser

210	215	220
Ser Val Val Glu Phe Cys	Asn Ala Ser Thr His	Asn Gln Glu Ala Pro
225	230	235
Asn Leu Gln Asn Gln Met Cys Ser	Leu Arg Ser Ala Trp Asp Val Ile	240
245	250	255
Thr Asp Ser Ala Asp Phe His His	Ser Phe Pro Met Asn Gly Thr Glu	260
260	265	270
Leu Pro Pro Pro Pro Thr Phe Ser	Leu Val Glu Ala Gly Asp Lys Val	275
275	280	285
Val Cys Leu Val Leu Asp Val Ser	Ser Lys Met Ala Glu Ala Asp Arg	290
290	295	300
Leu Leu Gln Leu Gln Gln Ala Ala	Glu Phe Tyr Leu Met Gln Ile Val	305
310	315	320
Glu Ile His Thr Phe Val Gly Ile Ala	Ser Phe Asp Ser Lys Gly Glu	325
325	330	335
Ile Arg Ala Gln Leu His Gln Ile	Asn Ser Asn Asp Asp Arg Lys Leu	340
340	345	350
Leu Val Ser Tyr Leu Pro Thr Thr	Val Ser Ala Lys Thr Asp Ile Ser	355
355	360	365
Ile Cys Ser Gly Leu Lys Lys Gly Phe	Glu Val Val Glu Lys Leu Asn	370
370	375	380
Gly Lys Ala Tyr Gly Ser Val Met Ile	Leu Val Thr Ser Gly Asp Asp	385
390	395	400
Lys Leu Leu Gly Asn Cys Leu Pro Thr	Val Leu Ser Ser Gly Ser Thr	405
410	415	420
Ile His Ser Ile Ala Leu Gly Ser Ser	Ala Ala Pro Asn Leu Glu Glu	425
425	430	435
Leu Ser Arg Leu Thr Gly Gly Leu Lys	Phe Phe Val Pro Asp Ile Ser	440
440	445	450
Asn Ser Asn Ser Met Ile Asp Ala Phe	Ser Arg Ile Ser Ser Gly Thr	455
455	460	465
Gly Asp Ile Phe Gln Gln His Ile Gln	Leu Glu Ser Thr Gly Glu Asn	470
470	475	480
Val Lys Pro His His Gln Leu Lys Asn	Thr Val Thr Val Asp Asn Thr	485
485	490	495
Val Gly Asn Asp Thr Met Phe Leu Val	Thr Trp Gln Ala Ser Gly Pro	500
500	505	510
Pro Glu Ile Ile Leu Phe Asp Pro Asp	Gly Arg Lys Tyr Thr Asn	515
515	520	525
Asn Phe Ile Thr Asn Leu Thr Phe Arg	Thr Ala Ser Leu Trp Ile Pro	530
530	535	540
Gly Thr Ala Lys Pro Gly His Trp Thr	Tyr Thr Leu Asn Asn Thr His	545
545	550	555
His Ser Leu Gln Ala Leu Lys Val Thr	Val Thr Ser Arg Ala Ser Asn	560
565	570	575
Ser Ala Val Pro Pro Ala Thr Val Glu	Ala Phe Val Glu Arg Asp Ser	580
580	585	590
Leu His Phe Pro His Pro Val Met Ile	Tyr Ala Asn Val Lys Gln Gly	595
600	605	610
Phe Tyr Pro Ile Leu Asn Ala Thr Val	Thr Thr Ala Thr Val Glu Pro Glu	615
615	620	625
Thr Gly Asp Pro Val Thr Leu Arg Leu	Leu Asp Asp Gly Ala Gly Ala	630
630	635	640
Asp Val Ile Lys Asn Asp Gly Ile Tyr	Ser Arg Tyr Phe Phe Ser Phe	645
645	650	655
Ala Ala Asn Gly Arg Tyr Ser Leu Lys	Val His Val Asn His Ser Pro	660
660	665	670
Ser Ile Ser Thr Pro Ala His Ser Ile	Pro Gly Ser His Ala Met Tyr	675

675	680	685
Val Pro Gly Tyr Thr Ala Asn Gly Asn Ile Gln Met Asn Ala Pro Arg		
690	695	700
Lys Ser Val Gly Arg Asn Glu Glu Glu Arg Lys Trp Gly Phe Ser Arg		
705	710	715
Val Ser Ser Gly Gly Ser Phe Ser Val Leu Gly Val Pro Ala Gly Pro		
720	725	730
His Pro Asp Val Phe Pro Pro Cys Lys Ile Ile Asp Leu Glu Ala Val		
735	740	745
Lys Val Glu Glu Glu Leu Thr Leu Ser Trp Thr Ala Pro Gly Glu Asp		
750	755	760
Phe Asp Gln Gly Gln Ala Thr Ser Tyr Glu Ile Arg Met Ser Lys Ser		
765	770	775
Leu Gln Asn Ile Gln Asp Asp Phe Asn Asn Ala Ile Leu Val Asn Thr		
780	785	790
Ser Lys Arg Asn Pro Gln Gln Ala Gly Ile Arg Glu Ile Phe Thr Phe		
795	800	805
Ser Pro Gln Ile Ser Thr Asn Gly Pro Glu His Gln Pro Asn Gly Glu		
810	815	820
Thr His Glu Ser His Arg Ile Tyr Val Ala Ile Arg Ala Met Asp Arg		
825	830	835
Asn Ser Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe		
840	845	850
Ile Pro Pro Asn Ser Asp Pro Val Pro Ala Arg Asp Tyr Leu Ile Leu		
855	860	865
Lys Gly Val Leu Thr Ala Met Gly Leu Ile Gly Ile Ile Cys Leu Ile		
870	875	880
Ile Val Val Thr His His Thr Leu Ser Arg Lys Lys Arg Ala Asp Lys		
885	890	895
Lys Glu Asn Gly Thr Lys Leu Leu		
900	905	910
915	920	

<210> 358

<211> 2773

<212> DNA

<213> Homo sapiens

<400> 358

catatgcagc	atcaccacca	tcaccacgga	gtacagcttc	aagacaatgg	gtataatgga	60
ttgctcattg	caattaatcc	tcaggtacct	gagaatcaga	acctcatctc	aaacattaag	120
gaaatgataa	ctgaagcttc	attttaccta	tttaagtcta	ccaagagaag	agtatttttc	180
agaaatataa	agattttta	acctgccaca	tggaagagcta	ataataacag	caaaataaaa	240
caagaatcat	atgaaaagcg	aaatgtcata	gtgactgact	ggatgtggcg	acatggagat	300
gatccataca	ccctacaata	cagaggggtg	ggaaaagagg	gaaaatacat	tcatttcaca	360
cctaatttcc	tactgaatga	taacttaaca	gctggctacg	gatcaagagg	ccgagtggtt	420
gtccatgaat	gggcccacct	cogttggggt	gtgttcgatg	agtataacaa	tgacaaacct	480
ttctacataa	atggggcaaaa	tcaaattaaa	gtgacaagggt	gttcattctga	catcacaggc	540
atttttttgt	gtgaaaaagg	tccttggccc	caagaaaact	gtattattag	taagcttttt	600
aaagaaggat	gcacotttat	ctacaatagc	accacaaaatg	caactgcatac	aataatgttc	660
atgcaaaagt	tatcttctgt	ggttgaattt	tgtaatgcaa	gtacccacaa	ccaagaagca	720
ccaaacctac	agaacagat	gtgcagcctc	agaagtgcac	gggatgtaat	cacagactct	780
gtgactcttc	accacagctt	tcccatgaac	gggactgagc	ttccacctcc	tccacattc	840
tcgcttgtag	aggctggtag	caaagtggtc	tgtttagtgc	tggtatgtgc	cagcaagatg	900
gcagaggctg	acagactcct	tcaactacaa	caagccgacg	aattttattt	gatgcagatt	960
gttgaaattc	atacctctgt	gggcattgac	agtttcgaca	gcaaaggaga	gatcacagcc	1020
cagctcaccc	aaattaacag	caatgatgat	cgaaagtgcg	tggtttcata	tctgcccacc	1080
actgtatcac	ctaaaacaga	catcagcatt	tgttcagggc	ttaagaaagg	atttgagggtg	1140

```

gttgaaaaac   tgaatggaaa   agcttatggc   tctgtgatga   tattagtac   cagcggagat   1200
gataagcttc   ttggcaattg   cttacccact   gtgctcagca   gtggttcaac   aattcactcc   1260
attgccctgg   gttcactctgc   agccccaact   ctggaggaaat   tatcacgtct   tacaggaggt   1320
ttaaagttct   ttgtttccaga   tatatcaaac   tccaatagca   tgattgatgc   ttccagtaga   1380
atttctctgt   gaactggaga   cattttccag   caacatatcc   agcttgaaag   tacaggtgaa   1440
aatgtcaaac   ctccaccatca   attgaaaaac   acagtgactg   tggataaatc   tgtgggcaac   1500
gacactatgt   ttctagttaac   gtggcaggcc   agtggtcctc   ctgagattat   attatttgat   1560
cctgatggac   gaaaaacta   cacaaataat   tttatcacca   atctaacttt   tcggcacagc   1620
agtcttttgg   ttccaggaaac   agctaagcct   gggcaactgga   cttaaccctc   gaacaatacc   1680
catcattctc   tgcaagccct   gaaagtgcac   gtgacctctc   gccctcccaa   ctacagctgtg   1740
ccccagacca   ctgtggaagc   ctttgtggaa   agagacagcc   tccattttcc   tcatcctgtg   1800
atgatttatg   ccaatgtgaa   acaggggatt   tatcccattc   ttaatgccac   tgtcactgcc   1860
acagttgagc   cagagactgg   agatcctggt   acgtcgagac   tccttgatga   tggagcaggt   1920
gctgatgtta   taaaaaatga   tggaaattac   tcgaggtatt   ttttctcctt   tgctgcaaat   1980
ggtagatata   gcttgaaagt   gcatgtcaat   cactctccca   gcataagcac   cccagcccaac   2040
tcatttcag   ggagtcaatg   tatgtatgta   ccaggttaca   cagcaaacgg   taatattcag   2100
atgaatgctc   caaggaaatc   agtaggcaga   aatgaggagg   agcgaaagt   gggcttttagc   2160
cgagtcaagct   caggagctc   cttttcagtg   ctgggagttc   cagctggccc   ccaccctgat   2220
gtgtttccac   catgcaaaat   tattgacctg   gaagctgtaa   aagtagaaga   ggaattgacc   2280
ctatcttggc   cagcacctgg   agaagacttt   gatcagggcc   aggotacaag   ctatgaataa   2340
agaatgagta   aaagtctaca   gaatatccaa   gatgacttta   acaatgctat   tttagtaaat   2400
acatacaagc   gaaatcctca   gcaagctggc   atcaggggaga   tatttacgtt   ctacccocaa   2460
atttccacga   attggactga   acatcagcca   aatggagaaa   cacatgaag   ccacagaatt   2520
tatgttgcaa   tacgagcaat   ggataggaaac   tccttacagt   ctgctgtatc   taacattgcc   2580
caggcgctc   tgttttatcc   cccaattct   gatcctgtac   ctgccagaga   ttatcttata   2640
ttgaaaggag   ttttaacagc   aatgggtttg   ataggaatca   tttgccttat   tatagtgtgt   2700
acacatcata   ctttaagcag   gaaaaagaga   gcagacaa   aagagaatgg   aacaaaatta   2760
ttataatgaa   ttc                                     2773

```

<210> 359

<211> 25

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 359

tggcagcccc tcttcttcaa gtggc

25

<210> 360

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 360

cgccagaatt catcaacaa atctgttagc acc

33

<210> 361

<211> 77

<212> PRT

<213> Homo sapiens

<400> 361

Met Gln His His His His His His Trp Gln Pro Leu Phe Phe Lys Trp

```

      1           5           10           15
Leu Leu Ser Cys Cys Pro Gly Ser Ser Gln Ile Ala Ala Ala Ser
      20
Thr Gln Pro Glu Asp Asp Ile Asn Thr Gln Arg Lys Lys Ser Gln Glu
      35
Lys Met Arg Glu Val Thr Asp Ser Pro Gly Arg Pro Arg Glu Leu Thr
      50
Ile Pro Gln Thr Ser Ser His Gly Ala Asn Arg Phe Val
      65           70           75

```

<210> 362
 <211> 244
 <212> DNA
 <213> Homo sapiens

```

<400> 362
catatgcagc atcaccacca tcaccaactgg cagccctctt tttcaagtg gctcttgtcc 60
tgtttgcctg ggagttctca aattgctgca gcagcctcca cccagcctga gcatgacatc 120
aatcacaga ggaagaagag tcaggaaaag atgagagaag ttacagactc tcctggggcga 180
ccccagagac ttaccattcc tcagacttct tcacatggtg ctaacagatt tgtttgatga 240
attc
244

```

<210> 363
 <211> 20
 <212> PRT
 <213> Homo sapiens

```

<400> 363
Met Trp Gln Pro Leu Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly
1           5           10           15
Ser Ser Gln Ile
20

```

<210> 364
 <211> 60
 <212> DNA
 <213> Homo sapiens

```

<400> 364
atgtggcagc cctcttctt caagtggctc ttgtctgtt gccctgggag ttctcaaatt 60

```

<210> 365
 <211> 20
 <212> PRT
 <213> Homo sapiens

```

<400> 365
Gly Ser Ser Gln Ile Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp
1           5           10           15
Ile Asn Thr Gln
20

```

<210> 366
 <211> 60

<212> DNA
<213> Homo sapiens

<400> 366
gggagttctc aaattgtctgc agcagcctcc acccagcctg aggatgacat caatacacag 60

<210> 367
<211> 20
<212> PRT
<213> Homo sapiens

<400> 367
Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu
1 5 10 15
Gln Ala Leu Lys
20

<210> 368
<211> 2343
<212> DNA
<213> Homo sapiens

<400> 368
attccggagc gtttgcggct tgccttcacg gccgctctcc cgcccctcct gggatctgtg 60
gggagctggg gggcccgagc cggcccgagc ccggagctgg cgagccgagc ggagacctgt 120
gcgccgcgcc tctgaggcgc agcatgtgaa cgaggagcgg catccagttg gggcgagacc 180
tctcagccggc cggggtatggc taccacggcc gagctcttcc agggagcctt tgtggcagat 240
gaatatattg aacgtcttgt atggagaacc ccaggaggag gctctagagg tggacctgaa 300
gctttttgat ctaaaagatt attagaagaa tttgtaaatc atattcagga actccagata 360
atggatgaaa gatttcagag gaaagtagag aaactagagc aacaatgtca gaaagaagcc 420
aaggaaattg ccaagaaggt acaagagctg cagaaaaagc atcaggttgc cttccaaacat 480
ttccaaagac tagatgagca cattagctat gttagcaacta aagctctgtca ccttggagac 540
cagttagagg gggtaaacac acccagacaa cgggcagttg aggtcagaaa attgatgaaa 600
tactttaatg agtttctaga tggagaattg aaatctgatg tttttacaaa ttctgaaaag 660
ataaaggagg cagcagacat cattcagaag ttgcacctaa ttgccaaga gttacctttt 720
gatagatttt cagaagttaa atccaaaatt gcaagtaaat accatgattt agaattgcag 780
ctgattcagg agtttaccag tgcctcaaga agaggtgaaa tctccagaat gagagaagta 840
gcagcagttt tacttcaatt taagggttat tccatttggt ttgatgttta tataaagcag 900
tgccaggagg gtgcttattt gagaaatgat atatttgaag acgctggagt actctgtcaa 960
agagtgaaca aacaagtgtg agatatcttc agtaatccag aaacagttct ggctaaactt 1020
attcaaaatg tatttgaatt caaactacag agttttgtga aagagcagtt agaagaatgt 1080
aggaagctcg atcgacagca atatctcaaa aatctctatg atctgtatc aagaaccacc 1140
aatctttcca ccaagctgat ggagtttaatt ttaggtactg ataaacagac ttcttctgtc 1200
aagctttatac aatccatttt catttctcat ttggagaact atattgaggt ggagacttga 1260
tatttgaaaa gcagaagtgc tatgatccta cagcgttatt atgattcgaa aaacatcaa 1320
aagagatcca ttggcacagg aggtattcaa gatttgaagg aaagaattag acagcgtacc 1380
aaccttaccac ttggggcaag tatcgatact catggggaga ctttctcatc caaagaagtg 1440
gtggttaatc ttttacaaga aaccaaaacaa gcctttgaaa gatgtcatag gctctctgat 1500
ccttctgact taccagaaggaa tgccttcaga atttttacca ttctgttggg atttttatgt 1560
attgagcata ttgattatgc tttggaaaca ggaacttgct gaattccctc ttcagatattc 1620
aggaatgcga atctttattt tttggacgtt gtgcaacagg ccaatactat ttatcatctt 1680
tttgaccaac agtttaatga tcaccttatg ccactaataa gctctctccc taagttatct 1740
gaatgccttc agaagaaaaa agaaataatt gaacaaatgg agatgaaatt ggaactctgc 1800
attgatagga cattaattgt tatgattgga cagatgaagc atattttggc tgcaagaacag 1860
aagaaaaacag atttttaagcc agaagatgaa aacaatgttt tgattcaata tactaatgcc 1920
tgtgtaaaaa tctgtgtcta cgttaagaaaa caagtggaga agattaaaaa ttcattggat 1980

```

gggaagaatg tggatacagt ttgatggaa cttggagtag gttttcatcg acttatctat 2040
gagcatcttc aacaatattc ctacagtgtg atgggtggca tgttgcccat ttgtgatgta 2100
gccgaatata ggaagtgtgc caaagacttc aagattccaa tggattatac tctttttgat 2160
actctgcatt cttcttgcaa tcttctggta gttgcccag ataattaaa gcaagctctg 2220
tcaggagaa aacttgctaa tctggacaag aatatacttc actcctctgt acaactctgt 2280
gtgattata gatctgccg ccttgcctga cacttcagct gagattgaat ttacaaggaa 2340
att

```

<210> 369

<211> 708

<212> PRT

<213> Homo sapiens

<400> 369

```

Met Ala Thr Thr Ala Glu Leu Phe Glu Glu Pro Phe Val Ala Asp Glu
1      5      10      15
Tyr Ile Glu Arg Leu Val Trp Arg Thr Pro Gly Gly Gly Ser Arg Gly
20     25     30
Gly Pro Glu Ala Phe Asp Pro Lys Arg Leu Leu Glu Glu Phe Val Asn
35     40     45
His Ile Gln Glu Leu Gln Ile Met Asp Glu Arg Ile Gln Arg Lys Val
50     55     60
Glu Lys Leu Glu Gln Gln Cys Gln Lys Glu Ala Lys Glu Phe Ala Lys
65     70     75     80
Lys Val Gln Glu Leu Gln Lys Ser Asn Gln Val Ala Phe Gln His Phe
85     90     95
Gln Glu Leu Asp Glu His Ile Ser Tyr Val Ala Thr Lys Val Cys His
100    105    110
Leu Gly Asp Gln Leu Glu Gly Val Asn Thr Pro Arg Gln Arg Ala Val
115    120    125
Glu Ala Gln Lys Leu Met Lys Tyr Phe Asn Glu Phe Leu Asp Gly Glu
130    135    140
Leu Lys Ser Asp Val Phe Thr Asn Ser Glu Lys Ile Lys Glu Ala Ala
145    150    155    160
Asp Ile Ile Gln Lys Leu His Leu Ile Ala Gln Glu Leu Pro Phe Asp
165    170    175
Arg Phe Ser Glu Val Lys Ser Lys Ile Ala Ser Lys Tyr His Asp Leu
180    185    190
Glu Cys Gln Leu Ile Gln Glu Phe Thr Ser Ala Gln Arg Arg Gly Glu
195    200    205
Ile Ser Arg Met Arg Glu Val Ala Ala Val Leu Leu His Phe Lys Gly
210    215    220
Tyr Ser His Cys Val Asp Val Tyr Ile Lys Gln Cys Gln Glu Gly Ala
225    230    235    240
Tyr Leu Arg Asn Asp Ile Phe Glu Asp Ala Gly Ile Leu Cys Gln Arg
245    250    255
Val Asn Lys Gln Val Gly Asp Ile Phe Ser Asn Pro Glu Thr Val Leu
260    265    270
Ala Lys Leu Ile Gln Asn Val Phe Glu Ile Lys Leu Gln Ser Phe Val
275    280    285
Lys Glu Gln Leu Glu Glu Cys Arg Lys Ser Asp Ala Glu Gln Tyr Leu
290    295    300
Lys Asn Leu Tyr Asp Leu Tyr Thr Arg Thr Thr Asn Leu Ser Ser Lys
305    310    315    320
Leu Met Glu Phe Asn Leu Gly Thr Asp Lys Gln Thr Phe Leu Ser Lys
325    330    335
Leu Ile Lys Ser Ile Phe Ile Ser Tyr Leu Glu Asn Tyr Ile Glu Val
340    345    350

```


Glu Thr Gly Tyr Leu Lys Ser Arg Ser Ala Met Ile Leu Gln Arg Tyr
 355 360 365
 Tyr Asp Ser Lys Asn His Gln Lys Arg Ser Ile Gly Thr Gly Gly Ile
 370 375 380
 Gln Asp Leu Lys Glu Arg Ile Arg Gln Arg Thr Asn Leu Pro Leu Gly
 385 390 395
 Pro Ser Ile Asp Thr His Gly Glu Thr Phe Leu Ser Gln Glu Val Val
 405 410 415
 Val Asn Leu Leu Gln Glu Thr Lys Gln Ala Phe Glu Arg Cys His Arg
 420 425 430
 Leu Ser Asp Pro Ser Asp Leu Pro Arg Asn Ala Phe Arg Ile Phe Thr
 435 440 445
 Ile Leu Val Glu Phe Leu Cys Ile Glu His Ile Asp Tyr Ala Leu Glu
 450 455 460
 Thr Gly Leu Ala Gly Ile Pro Ser Ser Asp Ser Arg Asn Ala Asn Leu
 465 470 475
 Tyr Phe Leu Asp Val Val Gln Gln Ala Asn Thr Ile Phe His Leu Phe
 485 490 495
 Asp Lys Gln Phe Asn Asp His Leu Met Pro Leu Ile Ser Ser Ser Pro
 500 505 510
 Lys Leu Ser Glu Cys Leu Gln Lys Lys Lys Glu Ile Ile Glu Gln Met
 515 520 525
 Glu Met Lys Leu Asp Thr Gly Ile Asp Arg Thr Leu Asn Cys Met Ile
 530 535 540
 Gly Gln Met Lys His Ile Leu Ala Ala Glu Gln Lys Lys Thr Asp Phe
 545 550 555
 Lys Pro Glu Asp Glu Asn Asn Val Leu Ile Gln Tyr Thr Asn Ala Cys
 565 570 575
 Val Lys Val Cys Ala Tyr Val Arg Lys Gln Val Glu Lys Ile Lys Asn
 580 585 590
 Ser Met Asp Gly Lys Asn Val Asp Thr Val Leu Met Glu Leu Gly Val
 595 600 605
 Arg Phe His Arg Leu Ile Tyr Glu His Leu Gln Gln Tyr Ser Tyr Ser
 610 615 620
 Cys Met Gly Gly Met Leu Ala Ile Cys Asp Val Ala Glu Tyr Arg Lys
 625 630 635
 Cys Ala Lys Asp Phe Lys Ile Pro Met Val Leu His Leu Phe Asp Thr
 645 650 655
 Leu His Ala Leu Cys Asn Leu Leu Val Val Ala Pro Asp Asn Leu Lys
 660 665 670
 Gln Val Cys Ser Gly Glu Gln Leu Ala Asn Leu Asp Lys Asn Ile Leu
 675 680 685
 His Ser Phe Val Gln Leu Arg Ala Asp Tyr Arg Ser Ala Arg Leu Ala
 690 695 700
 Arg His Phe Ser
 705

<210> 370

<211> 60

<212> DNA

<213> Homo sapiens

<400> 370

gtcaatcact ctcccagcat aagcacccca gccactcta ttccaggagg tcatgctatg 60

<210> 371

<211> 60
<212> DNA
<213> Homo sapiens

<400> 371
agtagaattt cctctggaac tggagacatt ttccagcaac atattcagct tgaagtaga 60

<210> 372
<211> 60
<212> DNA
<213> Homo sapiens

<400> 372
ccagagactg gagatcctgt tacgctgaga ctccctgatg atggagcagg tgctgatgtt 60

<210> 373
<211> 60
<212> DNA
<213> Homo sapiens

<400> 373
ttacagtctg ctgtatctaa cattgccag gcgcctctgt ttattcccc caattctgat 60

<210> 374
<211> 60
<212> DNA
<213> Homo sapiens

<400> 374
gctgtgcccc cagccactgt ggaagccttt gtggaagag acagcctcca ttttctcat 60

<210> 375
<211> 60
<212> DNA
<213> Homo sapiens

<400> 375
aaaaacacag tgactgtgga taatactgtg ggcaacgaca ctatgtttct agttacgtg 60

<210> 376
<211> 20
<212> PRT
<213> Homo sapiens

<400> 376
Leu Gln Ser Ala Val Ser Asn Ile Ala Gln Ala Pro Leu Phe Ile Pro
1 5 10 15
Pro Asn Ser Asp
20

<210> 377
<211> 20

<212> PRT

<213> Homo sapiens

<400> 377

Val Asn His Ser Pro Ser Ile Ser Thr Pro Ala His Ser Ile Pro Gly

1 5 10 15

Ser His Ala Met

20

<210> 378

<211> 20

<212> PRT

<213> Homo sapiens

<400> 378

Pro Glu Thr Gly Asp Pro Val Thr Leu Arg Leu Leu Asp Asp Gly Ala

1 5 10 15

Gly Ala Asp Val

20

<210> 379

<211> 20

<212> PRT

<213> Homo sapiens

<400> 379

Ala Val Pro Pro Ala Thr Val Glu Ala Phe Val Glu Arg Asp Ser Leu

1 5 10 15

His Phe Pro His

20

<210> 380

<211> 20

<212> PRT

<213> Homo sapiens

<400> 380

Ser Arg Ile Ser Ser Gly Thr Gly Asp Ile Phe Gln Gln His Ile Gln

1 5 10 15

Leu Glu Ser Thr

20

<210> 381

<211> 20

<212> PRT

<213> Homo sapiens

<400> 381

Lys Asn Thr Val Thr Val Asp Asn Thr Val Gly Asn Asp Thr Met Phe

1 5 10 15

Leu Val Thr Trp

20

<210> 382
<211> 20
<212> PRT
<213> Homo sapiens

<400> 382
Lys Pro Gly His Trp Thr Tyr Thr Leu Asn Asn Thr His His Ser Leu
1 5 10 15
Gln Ala Leu Lys
20

<210> 383
<211> 29
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 383
cggcgaattc atggattggg ggacgctgc 29

<210> 384
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 384
cggcctcgag tcacccdtct atcgaacct tctgc 35

<210> 385
<211> 32
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 385
cggcgaattc cacgaaccac tcgcaagttc ag 32

<210> 386
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 386
cggctcgagt tagcttgggc ctgtgattgc 30

<210> 387
<211> 20

<212> PRT

<213> Homo sapiens

<400> 387

Phe Phe Lys Trp Leu Leu Ser Cys Cys Pro Gly Ser Ser Gln Ile Ala

1 5 10 15

Ala Ala Ala Ser

20

<210> 388

<211> 19

<212> PRT

<213> Homo sapiens

<400> 388

Leu Ser Cys Cys Pro Gly Ser Ser Gln Ile Ala Ala Ala Ser Thr Gln

1 5 10 15

Pro Glu Asp

<210> 389

<211> 20

<212> PRT

<213> Homo sapiens

<400> 389

Ala Ala Ala Ala Ser Thr Gln Pro Glu Asp Asp Ile Asn Thr Gln Arg

1 5 10 15

Lys Lys Ser Ser Gln

20

<210> 390

<211> 20

<212> PRT

<213> Homo sapiens

<400> 390

Thr Gln Pro Glu Asp Asp Ile Asn Thr Gln Arg Lys Lys Ser Gln Glu

1 5 10 15

Lys Met Arg Glu

20

<210> 391

<211> 20

<212> PRT

<213> Homo sapiens

<400> 391

Asp Ile Asn Thr Gln Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val

1 5 10 15

Thr Asp Ser Pro

20

<210> 392
<211> 20
<212> PRT
<213> Homo sapiens

<400> 392
Arg Lys Lys Ser Gln Glu Lys Met Arg Glu Val Thr Asp Ser Pro Gly
1 5 10 15
Arg Pro Arg Glu
20

<210> 393
<211> 20
<212> PRT
<213> Homo sapiens

<400> 393
Glu Lys Met Arg Glu Val Thr Asp Ser Pro Gly Arg Pro Arg Glu Leu
1 5 10 15
Thr Ile Pro Gln
20

<210> 394
<211> 20
<212> PRT
<213> Homo sapiens

<400> 394
Val Thr Asp Ser Pro Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr
1 5 10 15
Ser Ser His Gly
20

<210> 395
<211> 19
<212> PRT
<213> Homo sapiens

<400> 395
Gly Arg Pro Arg Glu Leu Thr Ile Pro Gln Thr Ser Ser His Gly Ala
1 5 10 15
Asn Arg Phe

<210> 396
<211> 19
<212> PRT
<213> Homo sapiens

<400> 396
Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
1 5 10 15
Asp Leu Glu

<210> 397
<211> 20
<212> PRT
<213> Homo sapiens

<400> 397
Ser Glu Asn Ala Ala Pro Ser Asp Leu Glu Ser Ile Phe Lys Asp Ala
1 5 10 15
Lys Ile Pro Val
20

<210> 398
<211> 20
<212> PRT
<213> Homo sapiens

<400> 398
Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro Phe Leu Val
1 5 10 15
Lys Thr Gly Tyr
20

<210> 399
<211> 20
<212> PRT
<213> Homo sapiens

<400> 399
Ser Gly Pro Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro
1 5 10 15
Asp Glu Ser Trp
20

<210> 400
<211> 20
<212> PRT
<213> Homo sapiens

<400> 400
Ala Phe Val Asp Cys Pro Asp Glu Ser Trp Ala Leu Lys Ala Ile Glu
1 5 10 15
Ala Leu Ser Gly
20

<210> 401
<211> 20
<212> PRT
<213> Homo sapiens

<400> 401
Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His Gly
1 5 10 15

Lys Pro Ile Glu
20

<210> 402
<211> 20
<212> PRT
<213> Homo sapiens

<400> 402
Lys Ile Glu Leu His Gly Lys Pro Ile Glu Val Glu His Ser Val Pro
1 5 10 15
Lys Arg Gln Arg
20

<210> 403
<211> 20
<212> PRT
<213> Homo sapiens

<400> 403
Val Glu His Ser Val Pro Lys Arg Gln Arg Ile Arg Lys Leu Gln Ile
1 5 10 15
Arg Asn Ile Pro
20

<210> 404
<211> 20
<212> PRT
<213> Homo sapiens

<400> 404
Ile Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu
1 5 10 15
Val Leu Asp Ser
20

<210> 405
<211> 20
<212> PRT
<213> Homo sapiens

<400> 405
Ala Val Val Asn Val Thr Tyr Ser Ser Lys Asp Gln Ala Arg Gln Ala
1 5 10 15
Leu Asp Lys Lys
20

<210> 406
<211> 20
<212> PRT
<213> Homo sapiens

<400> 406

Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu Glu
1 5 10 15
Asn Phe Thr Leu
20

<210> 407
<211> 20
<212> PRT
<213> Homo sapiens

<400> 407
Asn Gly Phe Gln Leu Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro
1 5 10 15
Asp Glu Thr Ala
20

<210> 408
<211> 20
<212> PRT
<213> Homo sapiens

<400> 408
Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala Gln Gln Asn Pro Leu
1 5 10 15
Gln Gln Pro Arg
20

<210> 409
<211> 20
<212> PRT
<213> Homo sapiens

<400> 409
Ala Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly
1 5 10 15
Gln Arg Gly Ser
20

<210> 410
<211> 20
<212> PRT
<213> Homo sapiens

<400> 410
Gly Arg Arg Gly Leu Gly Gln Arg Gly Ser Ser Arg Gln Gly Ser Pro
1 5 10 15
Gly Ser Val Ser
20

<210> 411
<211> 20
<212> PRT
<213> Homo sapiens

<400> 411

Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys Pro Cys Asp
1 5 10 15
Leu Pro Leu Arg
20

<210> 412

<211> 20

<212> PRT

<213> Homo sapiens

<400> 412

Lys Gln Lys Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln
1 5 10 15
Phe Val Gly Ala
20

<210> 413

<211> 20

<212> PRT

<213> Homo sapiens

<400> 413

Leu Leu Val Pro Thr Gln Phe Val Gly Ala Ile Ile Gly Lys Glu Gly
1 5 10 15
Ala Thr Ile Arg
20

<210> 414

<211> 20

<212> PRT

<213> Homo sapiens

<400> 414

Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln Thr
1 5 10 15
Gln Ser Lys Ile
20

<210> 415

<211> 20

<212> PRT

<213> Homo sapiens

<400> 415

Asn Ile Thr Lys Gln Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu
1 5 10 15
Asn Ala Gly Ala
20

<210> 416

<211> 20

<212> PRT
 <213> Homo sapiens

<400> 416
 Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala Glu Lys Ser Ile Thr
 1 5 10 15
 Ile Leu Ser Thr
 20

<210> 417
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 417
 Ala Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala
 1 5 10 15
 Ala Cys Lys Ser
 20

<210> 418
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 418
 Pro Glu Gly Thr Ser Ala Ala Cys Lys Ser Ile Leu Glu Ile Met His
 1 5 10 15
 Lys Glu Ala Gln
 20

<210> 419
 <211> 20
 <212> PRT
 <213> Homo sapiens

<400> 419
 Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys Phe Thr Glu
 1 5 10 15
 Glu Ile Pro Leu
 20

<210> 420
 <211> 455
 <212> DNA
 <213> Homo sapiens

<400> 420
 gaagacatgc ttaacttccc ttcacettcc ttcgatgatg gggaagagtg ctgcaaccca 60
 gccctagcca acgccgcatg agagggagtg tgccgagggc ttctgagaag gttttctctca 120
 catctagaaa gaagcgctta agatgtggca gccctcttcc ttcaagtggc tcttgtcctg 180
 ttgccctggg agttctcaaa ttgctgcagc agcctccacc cagcctgagg atgacatcaa 240
 tacacagagg aagaagagtc aggaaaagat gagagaagtt acagactctc ctgggcgacc 300
 ccgagagctt accattcttc agacttcttc acatggtgct aacagatttg ttctctaaaag 360

taaagctcta gaggccgtca aattggcaat agaagccggg ttccaccata ttgattctgc 420
 acatgtttac aataatgagg agcaggttg actgg 455

<210> 421
 <211> 24
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 421
 actagtgtcc gcggtggcgc ctac 24

<210> 422
 <211> 34
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 422
 catgagaatt catcacatgc ccttgaaggc tccc 34

<210> 423
 <211> 161
 <212> PRT
 <213> Homo sapiens

<400> 423
 Met Gln His His His His His His His Thr Ser Val Arg Val Ala Ala
 1 5 10 15
 Tyr Phe Glu Asn Phe Leu Ala Ala Trp Arg Pro Val Lys Ala Ser Asp
 20 25 30
 Gly Asp Tyr Tyr Thr Leu Ala Val Pro Met Gly Asp Val Pro Met Asp
 35 40 45
 Gly Ile Ser Val Ala Asp Ile Gly Ala Ala Val Ser Ser Ile Phe Asn
 50 55 60
 Ser Pro Glu Glu Phe Leu Gly Lys Ala Val Gly Leu Ser Ala Glu Ala
 65 70 75 80
 Leu Thr Ile Gln Gln Tyr Ala Asp Val Leu Ser Lys Ala Leu Gly Lys
 85 90 95
 Glu Val Arg Asp Ala Lys Ile Thr Pro Glu Ala Phe Glu Lys Leu Gly
 100 105 110
 Phe Pro Ala Ala Lys Glu Ile Ala Asn Met Cys Arg Phe Tyr Glu Met
 115 120 125
 Lys Pro Asp Arg Asp Val Asn Leu Thr His Gln Leu Asn Pro Lys Val
 130 135 140
 Lys Ser Phe Ser Gln Phe Ile Ser Glu Asn Gln Gly Ala Phe Lys Gly
 145 150 155 160
 Met

<210> 424
 <211> 489
 <212> DNA

<213> Homo sapiens

<400> 424

```
atgcagcatc accaccatca ccaccacact agtgtccgcg tggcggccta ctttgaaaac 60
ttctctcgcg cgtggcgggc cgtgaaagcc tctgatggag attactacac ctgggctgta 120
ccgatgggag atgtaccaat ggatggtatc tctgttgctg atattggagc agccgtctct 180
agcattttta attctccaga ggaattttta ggcaaggccg tggggctcag tgcagaagca 240
ctaaacaatc agcaatatgc tgatgttttg tccaaggcct tggggaaaga agtccgagat 300
gcaaaagatta ccccggaagc ttctcgagaag ctgggattcc ctgcagcaaa ggaaatagcc 360
aatatgtgtc gtttctatga aatgaagcca gaccagagat tcaatctcac ccaccaacta 420
aatcccaaaag tcaaaaagctt cagccagttt atctcagaga accaggggag cttcaagggc 480
atgtgatga
```

<210> 425

<211> 32

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 425

aacaaactgt atatcggaag cctcagcgag aa

32

<210> 426

<211> 33

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 426

ccatagaatt cactacttcc gtcttgactg agg

33

<210> 427

<211> 586

<212> PRT

<213> Homo sapiens

<400> 427

```
Met Gln His His His His His Asn Lys Leu Tyr Ile Gly Asn Leu
1      5      10      15
Ser Glu Asn Ala Ala Pro Ser Asp Leu Glu Ser Ile Phe Lys Asp Ala
20     25     30
Lys Ile Pro Val Ser Gly Pro Phe Leu Val Lys Thr Gly Tyr Ala Phe
35     40     45
Val Asp Cys Pro Asp Glu Ser Trp Ala Leu Lys Ala Ile Glu Ala Leu
50     55     60
Ser Gly Lys Ile Glu Leu His Gly Lys Pro Ile Glu Val Glu His Ser
65     70     75     80
Val Pro Lys Arg Gln Arg Ile Arg Lys Leu Gln Ile Arg Asn Ile Pro
85     90     95
Pro His Leu Gln Trp Glu Val Leu Asp Ser Leu Leu Val Gln Tyr Gly
100    105    110
Val Val Glu Ser Cys Glu Gln Val Asn Thr Asp Ser Glu Thr Ala Val
115    120    125
Val Asn Val Thr Tyr Ser Ser Lys Asp Gln Ala Arg Gln Ala Leu Asp
```

130					135					140				
Lys	Leu	Asn	Gly	Phe	Gln	Leu	Glu	Asn	Phe	Thr	Leu	Lys	Val	Ala
145					150					155				160
Ile	Pro	Asp	Glu	Thr	Ala	Ala	Gln	Gln	Asn	Pro	Leu	Gln	Gln	Pro
				165						170				175
Gly	Arg	Arg	Gly	Leu	Gly	Gln	Arg	Gly	Ser	Ser	Arg	Gln	Gly	Ser
			180					185					190	
Gly	Ser	Val	Ser	Lys	Gln	Lys	Pro	Cys	Asp	Leu	Pro	Leu	Arg	Leu
		195					200					205		
Val	Pro	Thr	Gln	Phe	Val	Gly	Ala	Ile	Ile	Gly	Lys	Glu	Gly	Ala
	210					215					220			Thr
Ile	Arg	Asn	Ile	Thr	Lys	Gln	Thr	Gln	Ser	Lys	Ile	Asp	Val	His
225					230					235				Arg
Lys	Glu	Asn	Ala	Gly	Ala	Ala	Glu	Lys	Ser	Ile	Thr	Ile	Leu	Ser
			245						250					255
Pro	Glu	Gly	Thr	Ser	Ala	Ala	Cys	Lys	Ser	Ile	Leu	Glu	Ile	Met
			260					265					270	His
Lys	Glu	Ala	Gln	Asp	Ile	Lys	Phe	Thr	Glu	Glu	Ile	Pro	Leu	Lys
		275					280					285		Ile
Leu	Ala	His	Asn	Asn	Phe	Val	Gly	Arg	Leu	Ile	Gly	Lys	Glu	Gly
	290				295						300			Arg
Asn	Leu	Lys	Lys	Ile	Glu	Gln	Asp	Thr	Asp	Thr	Lys	Ile	Thr	Ile
305					310				315					320
Pro	Leu	Gln	Glu	Leu	Thr	Leu	Tyr	Asn	Pro	Glu	Arg	Thr	Ile	Thr
			325						330					335
Lys	Gly	Asn	Val	Glu	Thr	Cys	Ala	Lys	Ala	Glu	Glu	Glu	Ile	Met
		340						345					350	Lys
Lys	Ile	Arg	Glu	Ser	Tyr	Glu	Asn	Asp	Ile	Ala	Ser	Met	Asn	Leu
	355						360					365		Gln
Ala	His	Leu	Ile	Pro	Gly	Leu	Asn	Leu	Asn	Ala	Leu	Gly	Leu	Phe
	370				375					380				Pro
Pro	Thr	Ser	Gly	Met	Pro	Pro	Pro	Thr	Ser	Gly	Pro	Pro	Ser	Ala
	385				390				395					Met
Thr	Pro	Pro	Tyr	Pro	Gln	Phe	Glu	Gln	Ser	Glu	Thr	Glu	Thr	Val
			405					410					415	His
Leu	Phe	Ile	Pro	Ala	Leu	Ser	Val	Gly	Ala	Ile	Ile	Gly	Lys	Gln
	420							425					430	Gly
Gln	His	Ile	Lys	Gln	Leu	Ser	Arg	Phe	Ala	Gly	Ala	Ser	Ile	Lys
	435						440					445		Ile
Ala	Pro	Ala	Glu	Ala	Pro	Asp	Ala	Lys	Val	Arg	Met	Val	Ile	Ile
	450				455						460			Thr
Gly	Pro	Pro	Glu	Ala	Gln	Phe	Lys	Ala	Gln	Gly	Arg	Ile	Tyr	Gly
	465				470					475				Lys
Ile	Lys	Glu	Glu	Asn	Phe	Val	Ser	Pro	Lys	Glu	Glu	Val	Lys	Leu
			485					490					495	Glu
Ala	His	Ile	Arg	Val	Pro	Ser	Phe	Ala	Ala	Gly	Arg	Val	Ile	Gly
	500						505						510	Lys
Gly	Gly	Lys	Thr	Val	Asn	Glu	Leu	Gln	Asn	Leu	Ser	Ser	Ala	Glu
	515						520					525		Val
Val	Val	Pro	Arg	Asp	Gln	Thr	Pro	Asp	Glu	Asn	Asp	Gln	Val	Val
	530				535						540			Val
Lys	Ile	Thr	Gly	His	Phe	Tyr	Ala	Cys	Gln	Val	Ala	Gln	Arg	Lys
	545				550				555					560
Gln	Glu	Ile	Leu	Thr	Gln	Val	Lys	Gln	His	Gln	Gln	Gln	Lys	Ala
			565					570						Leu
Gln	Ser	Gly	Pro	Pro	Gln	Ser	Arg	Arg	Lys					575
			580					585						

<210> 428
 <211> 1764
 <212> DNA
 <213> Homo sapiens

<400> 428
 atgcagcatc accaccatca ccacaacaaa ctgtatatcg gaaacctcag cgagaacgcc 60
 gccccctcgg acctagaaga tatcttcaag gacgccaaaga tcccgggtgc gggacccttc 120
 ctgggtgaaga ctggctacgc gtctcgtggac tgcgccggacg agagctgggc cctcaaggcc 180
 atcgaggcgc tttcaggtaa aatagaactg caggggaaac ccatagaagt tgagcactcg 240
 gtcccaaaaa ggcaaggat tcggaaactt cagatcacga atatcccgcc tcatttcag 300
 tggggaggtgc tggatagttt actagtcag tatggatggg tggagagctg tgagcaagt 360
 aacactgact cggaaaactgc agttgttaaat gtaacctatt ccagtaagga ccaagctaga 420
 caagcactag acaaaactgaa tggatttcag ttgagaatt tcaccttgaa agtagcctat 480
 atccctgatg aaacggccgc ccagcaaaac cccttgacg agccccagg tgcgcggggg 540
 ctggggcaga ggggctcctc aaggcagggg tctccaggat ccgtatccaa gcagaaacca 600
 tgtgatttgc ctctgcgcct gctgggtccc acccaatttg ttggagccat catagggaaa 660
 gaaggtgcga ccattcggaa catcaccaaa cagaccaggt ctataactga tgtccacgt 720
 aaagaaaaat cgggggctgc tgagaagtgc attactatcc tctctactcc tgaaggcacc 780
 tctgcggcct gtaagtctat tctggagatt atgcataagg aagctcaaga tataaaattc 840
 acagaagaga tccccctgaa gatttttagct cataataact ttgttggagc tcttatttgt 900
 aaagaaggaa gaaatcttaa aaaaattgag caagacacag acactaaaat ccgatatct 960
 ccattgcagg aattgacgct gtataatcca gaacgcacta ttacagttaa aggcattgt 1020
 gagacatgtg ccaaatgtga ggaggagatc atgaagaaaa tcagggagatc ttatgaaaat 1080
 gatatttgct ctatgaatct tcaagcacat ttaattcctg gattaaatct gaacgccttg 1140
 ggtctgttcc caccaccttc agggatgcga cctcccaact ctcagcccatc ttoagccatg 1200
 actcctccct acccgagttg tgagcaatca gaaacggaga ctgttcatct gtttatccca 1260
 tctctatcag tctgtgccat catcggcaag cagggccagc acatcaagca gctttctcgc 1320
 ttgtcgtggg ctccaattaa gattgtccca gcggaagcac cagatgtcaa agtgaggatg 1380
 gtgattatca ctggaccacc agaggctcag tccaaggctc agggagaagt ttatggaaa 1440
 attaaagaag aaaaacttgt tagtcctaaa gaagaggtga aacttgaagc tcatatcaga 1500
 gtgccatcct ttgctgtcgg cagagttatt ggaaaaggag gcaaaacggt gaatgaact 1560
 cagaatttgt caagtgcaga agttgtgttc cctcgtgacc agacacctg tgagaatgac 1620
 caagtgtgtg tcaaaataac tggtaacttc tatgcttgcc aggttgccca gagaaaaatt 1680
 caggaaaattc tgactcaggt aaagcagcac caacaacaga aggcctctgc aagtgacc 1740
 cctcagtcga gacggaagta atga 1764

<210> 429
 <211> 35
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 429
 coattggaatt cattatttca atataagata atctc

35

<210> 430
 <211> 881
 <212> PRT
 <213> Homo sapiens

<400> 430
 Met Gln His His His His His Gly Val Gln Leu Gln Asp Asn Gly
 1 5 10 15
 Tyr Asn Gly Leu Leu Ile Ala Ile Asn Pro Gln Val Pro Glu Asn Gln

20				25				30							
Asn	Leu	Ile	Ser	Asn	Ile	Lys	Glu	Met	Ile	Thr	Glu	Ala	Ser	Phe	Tyr
	35						40					45			
Leu	Phe	Asn	Ala	Thr	Lys	Arg	Arg	Val	Phe	Phe	Arg	Asn	Ile	Lys	Ile
	50					55					60				
Leu	Ile	Pro	Ala	Thr	Trp	Lys	Ala	Asn	Asn	Asn	Ser	Lys	Ile	Lys	Gln
65					70					75					80
Glu	Ser	Tyr	Glu	Lys	Ala	Asn	Val	Ile	Val	Thr	Asp	Trp	Tyr	Gly	Ala
			85						90					95	
His	Gly	Asp	Asp	Pro	Tyr	Thr	Leu	Gln	Tyr	Arg	Gly	Cys	Gly	Lys	Glu
			100					105					110		
Gly	Lys	Tyr	Ile	His	Phe	Thr	Pro	Asn	Phe	Leu	Leu	Asn	Asp	Asn	Leu
			115				120					125			
Thr	Ala	Gly	Tyr	Gly	Ser	Arg	Gly	Arg	Val	Phe	Val	His	Glu	Trp	Ala
	130					135					140				
His	Leu	Arg	Trp	Gly	Val	Phe	Asp	Glu	Tyr	Asn	Asn	Asp	Lys	Pro	Phe
145					150					155					160
Tyr	Ile	Asn	Gly	Gln	Asn	Gln	Ile	Lys	Val	Thr	Arg	Cys	Ser	Ser	Asp
			165						170					175	
Ile	Thr	Gly	Ile	Phe	Val	Cys	Glu	Lys	Gly	Pro	Cys	Pro	Gln	Glu	Asn
			180					185					190		
Cys	Ile	Ile	Ser	Lys	Leu	Phe	Lys	Glu	Gly	Cys	Thr	Phe	Ile	Tyr	Asn
			195				200					205			
Ser	Thr	Gln	Asn	Ala	Thr	Ala	Ser	Ile	Met	Phe	Met	Gln	Ser	Leu	Ser
	210					215					220				
Ser	Val	Val	Glu	Phe	Cys	Asn	Ala	Ser	Thr	His	Asn	Gln	Glu	Ala	Pro
225					230					235					240
Asn	Leu	Gln	Asn	Gln	Met	Cys	Ser	Leu	Arg	Ser	Ala	Trp	Asp	Val	Ile
				245					250					255	
Thr	Asp	Ser	Ala	Asp	Phe	His	His	Ser	Phe	Pro	Met	Asn	Gly	Thr	Glu
			260					265					270		
Leu	Pro	Pro	Pro	Pro	Thr	Phe	Ser	Leu	Val	Glu	Ala	Gly	Asp	Lys	Val
	275						280					285			
Val	Cys	Leu	Val	Leu	Asp	Val	Ser	Ser	Lys	Met	Ala	Glu	Ala	Asp	Arg
	290					295					300				
Leu	Leu	Gln	Leu	Gln	Gln	Ala	Ala	Glu	Phe	Tyr	Leu	Met	Gln	Ile	Val
305					310					315					320
Glu	Ile	His	Thr	Phe	Val	Gly	Ile	Ala	Ser	Phe	Asp	Ser	Lys	Gly	Glu
				325					330					335	
Ile	Arg	Ala	Gln	Leu	His	Gln	Ile	Asn	Ser	Asn	Asp	Asp	Arg	Lys	Leu
			340					345					350		
Leu	Val	Ser	Tyr	Leu	Pro	Thr	Thr	Val	Ser	Ala	Lys	Thr	Asp	Ile	Ser
			355				360					365			
Ile	Cys	Ser	Gly	Leu	Lys	Lys	Gly	Phe	Glu	Val	Val	Glu	Lys	Leu	

			485			490			495
Val	Gly	Asn	Asp	Thr	Met	Phe	Leu	Val	Thr
			500					505	Thr
Pro	Glu	Ile	Ile	Leu	Phe	Asp	Pro	Asp	Gly
			515					520	Arg
Asn	Phe	Ile	Thr	Asn	Leu	Thr	Phe	Arg	Thr
			530				535		Ala
Gly	Thr	Ala	Lys	Pro	Gly	His	Trp	Thr	Tyr
			545				550		Thr
His	Ser	Leu	Gln	Ala	Leu	Lys	Val	Thr	Val
			565					570	Thr
Ser	Ala	Val	Pro	Pro	Ala	Thr	Val	Glu	Ala
			580					585	Phe
Leu	His	Phe	Pro	His	Pro	Val	Met	Ile	Tyr
			595				600		Ala
Phe	Tyr	Pro	Ile	Leu	Asn	Ala	Thr	Val	Thr
			610				615		Ala
Thr	Gly	Asp	Pro	Val	Thr	Leu	Arg	Leu	Leu
			625					630	Asp
Asp	Val	Ile	Lys	Asn	Asp	Gly	Ile	Tyr	Ser
			645					650	Arg
Ala	Ala	Asn	Gly	Arg	Tyr	Ser	Leu	Lys	Val
			660					665	His
Ser	Ile	Ser	Thr	Pro	Ala	His	Ser	Ile	Pro
			675				680		Gly
Val	Pro	Gly	Tyr	Thr	Ala	Asn	Gly	Asn	Ile
			690				695		Gln
Lys	Ser	Val	Gly	Arg	Asn	Glu	Glu	Arg	Lys
			705				710		Trp
Val	Ser	Ser	Gly	Gly	Ser	Phe	Ser	Val	Leu
			725					730	Gly
His	Pro	Asp	Val	Phe	Pro	Pro	Cys	Lys	Ile
			740					745	Asp
Lys	Val	Glu	Glu	Glu	Leu	Thr	Leu	Ser	Trp
			755				760		Thr
Phe	Asp	Gln	Gly	Gln	Ala	Thr	Ser	Tyr	Glu
			770				775		Ile
Leu	Gln	Asn	Ile	Gln	Asp	Asp	Phe	Asn	Asn
			785				790		Ala
Ser	Lys	Arg	Asn	Pro	Gln	Gln	Ala	Gly	Ile
			805					810	Arg
Ser	Pro	Gln	Ile	Ser	Thr	Asn	Gly	Pro	Glu
			820					825	His
Thr	His	Glu	Ser	His	Arg	Ile	Tyr	Val	Ala
			835				840		Ile
Asn	Ser	Leu	Gln	Ser	Ala	Val	Ser	Asn	Ile
			850				855		Ala
Ile	Pro	Pro	Asn	Ser	Asp	Pro	Val	Pro	Ala
			865				870		Arg
Lys									Asp

<210> 431

<211> 2646

<212> DNA

<213> Homo sapiens

```

<400> 431
atgcagcatc accaccatca ccacggagta cagcttcaag acaatgggta taatggattg 60
ctcattgcga ttaatctctc ggtacctgag aatcagaacc tcattctcaa cattaaaggaa 120
atgataacatc aagcttcatt ttacctattt aatgctacca agagaagagt atttttcaga 180
aatataaaga ttttaatacc tgccacatgg aaagctaata ataacagcaa aataaaacaa 240
gaatcatatg aaaaggcaaa tgtcatgatg actgactggt atggggcaca tggagatgat 300
ccatacaccc tcaaatcacg aggggttgga aaagaggaaa aatacacata ttccacacct 360
aatttctctc tgaatgataa cttaacagct ggctacggat cagcaggcgc agtgtttgtc 420
catgaatggg cccacctccg ttggggtgtg ttogatgagt ataacaatga caaaccttct 480
tacataaatg gccaataatc aattaaagtg acaaggtgtt catctgacat cagcggcatt 540
tttgttgatg aaaaagctcc ttgcccccaa gaaaactgta ttattagtaa cgtttttaa 600
gaaggatgca cttttatcta caatagcacc caaaatgcaa ctgcatcaat aatgttcatg 660
caaagtttat cttctgttgt tgaattttgt aatgcaagta cccacaacca agaagcacca 720
aacctacaga accagatgtg cagcctcaga agtgcatggg atgtaatcac agactctgct 780
gactttcacc acagcttccc catgaaacgg actgagcttc cacctctctc cacattctcg 840
ctgttagagg ctggtgacaa agtggcttgt ttagtctggt atgtgtccag caagatggca 900
gaggctgaca gactccttca actacacaaa gccgcagaat tttatttgat gcaagattgtt 960
gaattcata cctctgtggg cattgccagt ttogacaga aaggagaaat cagagctcct 1020
ctacacaaaa ttaacagcaa tgatgatcga aagtgtctgg tttcatatct gccaccact 1080
gtatcagcta aaacagacat cagcatttgt tcagggctta agaaaggatt ttgagtggtt 1140
gaaaaactga atgaaaaagc ttatggctct gtgatgatat tagtgaccag cggagatgat 1200
aagcttctgt gcaattgctt acccactgtg ctacgacgtg gtccaacat tcactccatt 1260
gccttgggtt catctgcagc cccaaactcg gaggaattat cacgtctctac aggaggttta 1320
aagttctttg ttccagatat atcaaacctc aatagcatga ttgatgcttt cagtagaatt 1380
tcctctggaa ctggagacat ttccagcaa catattcagc ttgaaagtac aggtgaaaat 1440
gtcaaacctc accatcaatt gaaaaacaca gtgactgtgg ataactgtg gggcaacgac 1500
actatgttcc tagttacgtg gcaggccagt ggtcctctcg agatttatatt atttgatcct 1560
gatggagcaa aatactacac aaataatttt atcaccatc taacttttgc gacagctagt 1620
ctttgtgttc caggaaacgc taagcctggg cactggactt acaccctgaa caatacccat 1680
cattctctgc aagccctgaa agtgacagt acctctcgcg cctccaactc agctgtgcc 1740
ccagccactg tggaaagcct ttgtgaaaga gacagcctcc attttctca tcctgtgatg 1800
atttatgcca atgtgaaaca gggattttat cccattctta atgcactgt cactgccaca 1860
gttgagccag agactggaga tctgtttaog ctgagactcc ttgatgatgg agcaggtgct 1920
gatgtttata aaaatgatgg aattttactg aggtattttt tctcctttgc tgcaaatggt 1980
agatatagct tgaagtgcga tgtcaatcac tctccagca taagcaccoc agccactct 2040
attccaggga gtcactgtat gtatgtacca ggttacacg caaacggtaa tattcagatg 2100
aatgctccaa ggaatcagt aggcagaaat gaggaggagc gaaagtgggg ctttagccga 2160
gcagctcagc gaggctcctt ttcagtgtcg ggagtccag ctggccccc cctgatgtg 2220
tttccaccat gcaaaattat tgacctggaa gctgtaaaag tagaagagga attgacccta 2280
tcttggaacg cactggaga agactttgat caggggcag ctacaagta tgaataaga 2340
atgagtaaaa gtctacagaa tatccaagat gactttaaca atgctatttt agtaaatata 2400
tcaaaagcaa atcctcagca agctggcatc agggagatat ttactgtctc accccaaatt 2460
tcacgaaatg gactgaacca tcaggccaaat ggagaaacac atgaaggcca cagaatttat 2520
gttgcaatca gagcaatgga taggaactcc ttacagtctg ctgtatctaa cttgtcccag 2580
gcgcctctgt ttattccccc caattctgat cctgtacctg ccagagagata tcttatattg 2640
aataaa

```

<210> 432

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 432

gcgctgtcgt agtcattaat attcatcaga aaatgg

36

<210> 433
 <211> 371
 <212> PRT
 <213> Homo sapiens

<400> 433

```

Met Gln His His His His His His Trp Gln Pro Leu Phe Phe Lys Trp
 1          5          10          15
Leu Leu Ser Cys Cys Pro Gly Ser Ser Gln Ile Ala Ala Ala Ser
 20          25          30
Thr Gln Pro Glu Asp Asp Ile Asn Thr Gln Arg Lys Lys Ser Gln Glu
 35          40          45
Lys Met Arg Glu Val Thr Asp Ser Pro Gly Arg Pro Arg Glu Leu Thr
 50          55          60
Ile Pro Gln Thr Ser Ser His Gly Ala Asn Arg Phe Val Pro Lys Ser
 65          70          75
Lys Ala Leu Glu Ala Val Lys Leu Ala Ile Glu Ala Gly Phe His His
 85          90          95
Ile Asp Ser Ala His Val Tyr Asn Asn Glu Glu Gln Val Gly Leu Ala
100          105          110
Ile Arg Ser Lys Ile Ala Asp Gly Ser Val Lys Arg Glu Asp Ile Phe
115          120          125
Tyr Thr Ser Lys Leu Trp Ser Asn Ser His Arg Pro Glu Leu Val Arg
130          135          140
Pro Ala Leu Glu Arg Ser Leu Lys Asn Leu Gln Leu Asp Tyr Val Asp
145          150          155
Leu Tyr Leu Ile His Phe Pro Val Ser Val Lys Pro Gly Glu Glu Val
165          170          175
Ile Pro Lys Asp Glu Asn Gly Lys Ile Leu Phe Asp Thr Val Asp Leu
180          185          190
Cys Ala Thr Trp Glu Ala Met Glu Lys Cys Lys Asp Ala Gly Leu Ala
195          200          205
Lys Ser Ile Gly Val Ser Asn Phe Asn His Arg Leu Leu Glu Met Ile
210          215          220
Leu Asn Lys Pro Gly Leu Lys Tyr Lys Pro Val Cys Asn Gln Val Glu
225          230          235
Cys His Pro Tyr Phe Asn Gln Arg Lys Leu Leu Asp Phe Cys Lys Ser
245          250          255
Lys Asp Ile Val Leu Val Ala Tyr Ser Ala Leu Gly Ser His Arg Glu
260          265          270
Glu Pro Trp Val Asp Pro Asn Ser Pro Val Leu Leu Glu Asp Pro Val
275          280          285
Leu Cys Ala Leu Ala Lys Lys His Lys Arg Thr Pro Ala Leu Ile Ala
290          295          300
Leu Arg Tyr Gln Leu Gln Arg Gly Val Val Val Leu Ala Lys Ser Tyr
305          310          315
Asn Glu Gln Arg Ile Arg Gln Asn Val Gln Val Phe Glu Phe Gln Leu
325          330          335
Thr Ser Glu Glu Met Lys Ala Ile Asp Gly Leu Asn Arg Asn Val Arg
340          345          350
Tyr Leu Thr Leu Asp Ile Phe Ala Gly Pro Pro Asn Tyr Pro Phe Ser
355          360          365
Asp Glu Tyr
370

```

<210> 434
 <211> 1119

<212> DNA

<213> Homo sapiens

<400> 434

atgcagcatc	accaccatca	ccactggcag	ccccctctct	tcaagtggtc	cttgtcctgt	60
tgccctggga	gtctctcaat	tgctgcagca	gcctccacc	agcctgagga	tgacatcaat	120
acacagagga	agaagagtca	ggaaaagatg	agagaagtta	cagactctcc	tgggcgaccc	180
cgagagctta	ccattctctca	gactctctca	catggtgcta	acagatttgt	tcctaaaagt	240
aaagctctag	aggccgtcaa	attggcaata	gaagccgggt	tcacccat	tgattctgca	300
catgtttaca	ataatgagga	gcaggttgga	ctggccatcc	gaagcaagat	tcagatggc	360
agtgtgaaga	gagaagacat	attctacact	tcaaagcttt	ggagcaattc	ccatcgacca	420
gagttggtcc	gaccagcctt	ggaaaggtca	ctgaaaaatc	ttcaattgga	ctatgttgac	480
ctctatctta	ttcatittcc	agtgtctgta	aagccagggt	aggaagtgat	cccaaaagat	540
gaaaaaggaa	aaatactatt	tgacacagtg	gatctctgtg	ccacatggga	ggccatggag	600
aagtgtaaag	atgcaggatt	ggccaagtcc	atcggggtgt	ccaacttcaa	ccacaggctg	660
ctggagatga	tcctcaacaa	gccagggtcc	aagtacaagc	ctgtctgcaa	ccaggtggaa	720
tgctatcctt	acttcaacca	gagaaaaactg	ctggatttct	gcaagtcaaa	agacattggt	780
ctggttgctt	atagtgtctt	gggatcccat	cgagaagaac	catgggtgga	ccogaactcc	840
ccggtgtcct	tggaggacc	agtcctttgt	gccttggcaa	aaaagcacaa	gcgaacccca	900
gccttgattg	ccctgcgcta	ccagctgcag	cgtaggggtt	tggtcctggc	caagagctac	960
aatgagcagc	gcatacagca	gaacgtgcag	gtgtttgaat	tcacgttgac	ttcagaggag	1020
atgaaagcca	tagatggcct	aaacagaaat	gtgcgatatt	tgacccttga	tatttttgc	1080
ggccccctca	attatccatt	ttctgatgaa	tattaatga			1119

<210> 435

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 435

ggatccgcgc	ccaccatgac	atccattcga	gctgta	36
------------	------------	------------	--------	----

<210> 436

<211> 27

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 436

gtcgactcag	ctggaccaca	gccgcag	27
------------	------------	---------	----

<210> 437

<211> 37

<212> DNA

<213> Artificial Sequence

<220>

<223> Primer

<400> 437

ggatccgcgc	ccaccatgga	ctcctggacc	ttctgct	37
------------	------------	------------	---------	----

<210> 438

<211> 27
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> Primer

<400> 438
 gtcgactcag aaatcctttc tcttgac

27

<210> 439
 <211> 933
 <212> DNA
 <213> Homo sapiens

<400> 439
 atggactcct ggaccttctg ctgtgtgtcc ctttgcattc tggtagcaaa gcacacagat 60
 gctggagtta tccagtcacc coggcagcag gtgacagaga tgggacaaga agtgactctg 120
 agatgtaaac caatttcagg acacgactac cttttctggt acagacagac catgatgcgg 180
 ggactggagt tgctcattta ctttaacaac aacgttcoga tagatgattc agggatgcc 240
 gagatcgat tctcagctaa gatgcctaatt gcatcattct ccactctgaa gatccagccc 300
 tcagaaccca gggactcagc tgtgtacttc tgtgccagca gtttagttgg agcaaacact 360
 gaagctttct ttggacaagg caccagactc acagtgttag aggacctgaa caaggtgttc 420
 ccaccggagg tgcgtgtgtt tgagccatca gaagcagaga tctccacac ccaaaaggcc 480
 acactgggtg cctctggcac aggccttctc cctgaccacg tggagctgag ggtgtgggtg 540
 aatgggaagg aggtgcacag tggggtcagc acggaccgcg agccctcaga ggaagcagcc 600
 gcctcaatg actccagata ctgcctgagc agccgcctga gggctctggc cactctctg 660
 cagaaccccc gcaaccactt cgcctgcaa gtccagtctc acgggctctc ggagaatgac 720
 gagtggaccc aggatagggc caaacccgtc acccagatcg tcaagcccca gccctgggggt 780
 agagcagact gtggctttac ctgggtgtcc taccagcaag gggctctctc tgccaccatc 840
 ctctatgaga tctctgtagg gaaggccacc ctgtatgctg tctgtgtcag cgcctctgtg 900
 ttgatggcca tggccaagag aaaggatttc tga 933

<210> 440
 <211> 822
 <212> DNA
 <213> Homo sapiens

<400> 440
 atgacatcca ttgcagctgt atttataatc ctgtggctgc agctggactt ggtgaatgga 60
 gagaatgtgg agcagatcc ttcaaccctg agtgctcagg agggagacag cgtgtttatc 120
 aagtgtactt attcagacag tgctccaacac tacttccctt ggtataagca agaacttgga 180
 aaagacacct agcttattat agacattcgt tcaaatgtgg cgcaaaagaa agaccaacga 240
 attgtctgta cattgaacaa gacagccaaa catttctccc tgcaatcac agagaccacaa 300
 cctgaagact gcctgtctta cttctgtgca gcaagtatac tgaacaccgg taaccagttc 360
 tatttttgga caggggacaag tttgacggtc attccaaata tccagaaccc tgacctgtcc 420
 gttgaccagc tgagacact taaatccagt gacaagctct totgcctatt caccgatttt 480
 gattctcaaa caaatgtgtc acaaatgaag gattctgatg tgtatatac agacaaaact 540
 gtgctagaca tgaggtctat ggactccaag agcaacagtg ctgtggcctg gagcaacaaa 600
 tctgaacttg catgtgcaaa cgcctccaac aacagcatta ttccagaaga caacttcttc 660
 ccagcccgag aaagtctctg tgatgtcaag ctggctgaga aaagctttga aacagatagc 720
 aaactaaact ttcaaaacct gtcagtgtatt ggggttcgaa tctctctctt gaaagtggcc 780
 ggggttaatc tgctcatgac gctgoggctg tggctcagct ga 822

<210> 441
 <211> 2311
 <212> DNA

<213> Homo sapiens

<400> 441

attttaa	tc	atgatttggtt	ctgtcttcac	ctgttttgggt	gaggtttgtg	60
aagatgtgtg	gtttgtctcag	gaagagattt	agacatgctt	gcttacccag	actccagaaa	120
tctgtccctg	tctgtctcag	tctgttctct	gtgtttgtgt	catctgtctt	ttccagagca	180
aagcccccag	agtagaagat	ggattggggc	acgtcgcaga	cga	ctctcgtgg	240
aaacactca	ccagatcagt	aaagatctgg	ctcaacgtct	ttcttcattt	tgcgatattg	300
atctctgttg	tggctgcmaa	ggaggtgtgtg	ggagatgagc	agggccattt	tgtcttccaac	360
accttcgaac	cagctgtgca	cagactgtgc	tacgatcatc	acttcccatt	ctccacattc	420
cggtctatgg	ccctcgaact	gattctctgt	tcaccagcca	cgctctcagt	ggccatgcac	480
tgtgctccac	ggagacatga	gaagaagagg	aagtttcaac	agggggagat	aaagagttaa	540
tttaaggaca	tcgaggagat	caaaacccag	aagttccgca	tcgaaggctc	ccctgtggtg	600
acctacaaca	cagacatctt	cttcgggttc	attctcgaag	ccgccttcac	tgaactgtct	660
tatttcagtt	acagacggtt	ctccatgcag	cggtctgtga	agctgaacgc	tgcggtcttg	720
cccaacactc	tggactgctt	tgtgtcccg	cccaagggag	agactgtctt	cacagttgtc	780
atctgttcag	tgtctggagt	tgtcatctgt	ctgaattgta	ctgaattgtt	tattttgtca	840
aatagatatt	gtctgtggaa	ctgcaaaaag	ccagttttaa	cgattgccta	tgtgttaagt	900
taagaaatga	acgcatcagc	agggatgaag	acacccgtgc	tcagttgcca	aggtctacgt	960
gccgcatttt	cccaacacga	agattctgc	cttaaatgca	accattttgaa	accocctgtag	1020
gcttcagggt	aaactccaga	tgcaccaagt	agctctgtct	ccctaagaac	ctcaaaacaa	1080
ggccaaatc	tatgctctgc	tttaattttc	ttcaactaag	ttagttccac	tgagacacca	1140
tgtctgttag	tggttatctt	gtaagggttc	tccaattttt	aaacagagtt	tatcggcatt	1200
gggtttcttc	tcttagggca	agagaaaaaa	gcgaagtttc	acagagagca	cagagaaggt	1260
tgtgtgtctc	tcctgggggt	cttttttgca	acttccccca	cgtaaaaggt	gaacattgtt	1320
ttcttcattc	tcgtttgaa	tttttaattc	tacaagtgtc	caaaagtacc	agtgctctaa	1380
actctgtttc	actttttgga	agtgaaaact	tgttgattat	atagggtatt	ttgatgtaaa	1440
gagtttcttg	ataccattat	atgttcccc	tgtttcagag	gctcagattg	taatatgtaa	1500
atggttatgc	attcgctact	atgtattaat	tgaatatatt	gtcttttggg	tatgaatact	1560
ttgcagaca	gcgtgagag	gcgtctgtgt	gtattctatt	ttgtctatgc	acctcaacac	1620
ttttagtcct	caatgcagat	agacagacta	gaagtttcta	tgtggtctat	gatagaactt	1680
ggcctcatgt	caaatattat	atgtaatitt	ttgtaaagaa	tcacagatgt	atgtcacatt	1740
aaactactac	tgtaatgaca	ggcctgtcca	acacatctcc	cttttccatg	cttgggttag	1800
cagcatcgga	aagaacgctg	atttaaaagg	gttgagctgg	gaattttctg	gacacagatt	1860
ctttaaattg	ggagacagaaa	atggggccca	ggggagggtg	agattttatg	cgtaaaaact	1920
gagtttggaa	agactggact	ctaaattctg	ttgattataa	atgagctttg	tctacctcca	1980
aaagttttgt	tggcttacc	ccttcagcct	coaatttttt	aaagtgaatt	ataactata	2040
acaattgaaa	agataagaag	ctaaagttta	gataaatttt	gagcagatct	ataggaagat	2100
tgaacctgaa	tattgccatt	atgcttgaca	agatttccaa	aaatgggtac	tccacattct	2160
tcagctgagg	taagtattat	ctcgttgtca	agaaatagat	tttaaaagac	ttttgtaatt	2220
ataaagaata	gctttaatga	tatgctgtga	actaaaataa	ttttgtaatg	tatcaaatc	2280
atttaaaaca	ttaaaataata	attctctata	t			2340

<210> 442

<211> 226

<212> PRT

<213> Homo sapiens

<400> 442

Met Asp Trp Gly Thr Leu Gln Thr Ile Leu Gly Gly Val Asn Lys His
5 10 15

Ser Thr Ser Ile Gly Lys Ile Trp Leu Thr Val Leu Phe Ile Phe Arg
20 25 30

Ile Met Ile Leu Val Val Ala Ala Lys Glu Val Trp Gly Asp Glu Gln
35 40 45

Ala Asp Phe Val Cys Asn Thr Leu Gln Pro Gly Cys Lys Asn Val Cys
 50 55 60
 Tyr Asp His Tyr Phe Pro Ile Ser His Ile Arg Leu Trp Ala Leu Gln
 65 70 75 80
 Leu Ile Phe Val Ser Ser Pro Ala Leu Leu Val Ala Met His Val Ala
 85 90 95
 Tyr Arg Arg His Glu Lys Lys Arg Lys Phe Ile Lys Gly Glu Ile Lys
 100 105 110
 Ser Glu Phe Lys Asp Ile Glu Glu Ile Lys Thr Gln Lys Val Arg Ile
 115 120 125
 Glu Gly Ser Leu Trp Trp Thr Tyr Thr Ser Ser Ile Phe Phe Arg Val
 130 135 140
 Ile Phe Glu Ala Ala Phe Met Tyr Val Phe Tyr Val Met Tyr Asp Gly
 145 150 155 160
 Phe Ser Met Gln Arg Leu Val Lys Cys Asn Ala Trp Pro Cys Pro Asn
 165 170 175
 Thr Val Asp Cys Phe Val Ser Arg Pro Thr Glu Lys Thr Val Phe Thr
 180 185 190
 Val Phe Met Ile Ala Val Ser Gly Ile Cys Ile Leu Leu Asn Val Thr
 195 200 205
 Glu Leu Cys Tyr Leu Leu Ile Arg Tyr Cys Ser Gly Lys Ser Lys Lys
 210 215 220
 Pro Val
 225

<210> 443
 <211> 23
 <212> PRT
 <213> Homo sapiens

<400> 443
 Val Lys Leu Cys Gly Ile Asp Pro Cys Pro Asn Leu Val Asp Cys Phe
 5 10 15
 Ile Ser Arg Pro Gly Cys Gly
 20

<210> 444
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> PCR primer

<400> 444
caatcaggca tgcacaacaa actgtatatc ggaaac

36

<210> 445
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> PCR primer

<400> 445
cgccaagatc ttcattactt ccgtcttgac

30

<210> 446
<211> 579
<212> PRT
<213> Homo sapiens

<400> 446
Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
5 10 15
Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro
20 25 30
Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
35 40 45
Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
50 55 60
Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile
65 70 75 80
Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
85 90 95
Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln
100 105 110
Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser
115 120 125
Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
130 135 140
Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala
145 150 155 160
Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Gly Leu Gly Gln
165 170 175
Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly
 195 200 205
 Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
 210 215 220
 Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala
 225 230 235 240
 Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala
 245 250 255
 Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys
 260 265 270
 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Phe Val
 275 280 285
 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln
 290 295 300
 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu
 305 310 315 320
 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys
 325 330 335
 Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu
 340 345 350
 Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu
 355 360 365
 Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro
 370 375 380
 Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe
 385 390 395 400
 Glu Gln Ser Glu Thr Glu Thr Val His Leu Phe Ile Pro Ala Leu Ser
 405 410 415
 Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser
 420 425 430
 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp
 435 440 445
 Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe
 450 455 460
 Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val
 465 470 475 480
 Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser
 485 490 495
 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu
 500 505 510

Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr
 515 520 525
 Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr
 530 535 540
 Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val
 545 550 555 560
 Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
 565 570 575
 Arg Arg Lys

<210> 447
 <211> 1743
 <212> DNA
 <213> Homo sapiens

<400> 447
 atgaacaac tgtatatcgg aaacctcagc gagaacgcgc cccctcggga cctagaaagt 60
 atcttcaag acgccaagat cccggtgtcg ggacccttcc tggtagaac tggctaacgc 120
 ttctgtgact gcccggaaga gagctgggccc ctcaaggcca tcgaggcgct ttcaaggtaa 180
 atagaactgc acgggaaacc catagaagtt gagcactcgg tcccaaaaag gcaaggatt 240
 cggaaacttc agatacgaat tatcccgctt catttacagt gggagggtct ggatagttta 300
 ctagtccagt atggagtggt ggagagctgt gagcaagtga acactgactc ggaaactgca 360
 gttgtaaatg taacctatcc cagtaaggac caagctagac aagcactaga caaactgaat 420
 ggatttcagt tagagaattt caccttgaaa gtacactata tccctgatga aacggccgcc 480
 cagcaaaacc ccttcgagca gcccccgagg ccccgggggc ttgggcagag gggctcctca 540
 aggcaggggg ctccaggatc cgtatccaag cagaaaccaa gtgatttgcc tctgcgcctg 600
 ctggttccca cccaatttgt tggagccatc ataggaagag aagggtccac cattcggaac 660
 atcaccaaac agaccagctc taaaatcgat gtccaccgta aagaaaatgc gggggctgct 720
 gagaagtoga ttactatcct ctctactcct gaaggcacct ctgcggcttg taagtctatt 780
 ctggagatta tgcataagga agctcaagat ataaaaatca cagaagagat ccccttgaag 840
 attttagctc ataataactt tgttggacgt ctatttggtt aagaaggaga aaactctaaa 900
 aaaaattgag aagcaccata cactaaaaatc acgatattct cattgcagga attgacgctg 960
 tataatccag aacgcactat tacagttaaa ggcaatgttg agacatgtgc caaagctgag 1020
 gaggagatca tgaagaaatc cagggagctt tatgaaaatg atattgtctc tatgaattct 1080
 caagcacatt taattcctgg attaaatctg aacgccttgg gctgtgtccc acccaactca 1140
 gggatgccac ctcccaacct agggccccct tcagccatga ctccctccta cccgcagttt 1200
 gagcaatcag aaacggagac tgttcatctg tttatccag ctctatcagt cgggtgccat 1260
 atcgccagac agggccagca catcaagcag ctttctcgct ttgctggagc ttcaattaag 1320
 attgtccagc cggaagcacc agatgtctaa gtgaggatgg tgattatcac tggaccacca 1380
 gaggtccagt tcaaggctca gggaagaatt tatggaaaaa ttaagaaga aaactttgtt 1440
 agtctctaaag aagaggtgaa acttgaagct catatcagag tgccatcctt tgcgtctggc 1500
 agagttattg gaaaaggagg caaacgggtg aatgaacttc agaattttgc aagtgcagaa 1560
 gttgtgtctc ctctgtgacc gacacctgat gagaatgacc aagtgttgtt caaaataact 1620
 ggtcactctt atgcttgcca ggttgcccag agaaaaatc aggaattctt gactcaggtt 1680
 aagcagcacc aacaacagaa ggtctctgaa agtggaccac ctcaagtaag acggaagtaa 1740
 tga 1743

<210> 448
 <211> 35
 <212> DNA

<213> Artificial Sequence

<220>

<223> PCR primer

<400> 448

cgtactagca tatgaacaaa ctgtatatcg gaaac

35

<210> 449

<211> 579

<212> PRT

<213> Homo sapiens

<400> 449

Met Asn Lys Leu Tyr Ile Gly Asn Leu Ser Glu Asn Ala Ala Pro Ser
5 10 15

Asp Leu Glu Ser Ile Phe Lys Asp Ala Lys Ile Pro Val Ser Gly Pro
20 25 30

Phe Leu Val Lys Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser
35 40 45

Trp Ala Leu Lys Ala Ile Glu Ala Leu Ser Gly Lys Ile Glu Leu His
50 55 60

Gly Lys Pro Ile Glu Val Glu His Ser Val Pro Lys Arg Gln Arg Ile
65 70 75 80

Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu Val
85 90 95

Leu Asp Ser Leu Leu Val Gln Tyr Gly Val Val Glu Ser Cys Glu Gln
100 105 110

Val Asn Thr Asp Ser Glu Thr Ala Val Val Asn Val Thr Tyr Ser Ser
115 120 125

Lys Asp Gln Ala Arg Gln Ala Leu Asp Lys Leu Asn Gly Phe Gln Leu
130 135 140

Glu Asn Phe Thr Leu Lys Val Ala Tyr Ile Pro Asp Glu Thr Ala Ala
145 150 155 160

Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly Gln
165 170 175

Arg Gly Ser Ser Arg Gln Gly Ser Pro Gly Ser Val Ser Lys Gln Lys
180 185 190

Pro Cys Asp Leu Pro Leu Arg Leu Leu Val Pro Thr Gln Phe Val Gly
195 200 205

Ala Ile Ile Gly Lys Glu Gly Ala Thr Ile Arg Asn Ile Thr Lys Gln
210 215 220

Thr Gln Ser Lys Ile Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala
225 230 235 240

Glu Lys Ser Ile Thr Ile Leu Ser Thr Pro Glu Gly Thr Ser Ala Ala
 245 250 255
 Cys Lys Ser Ile Leu Glu Ile Met His Lys Glu Ala Gln Asp Ile Lys
 260 265 270
 Phe Thr Glu Glu Ile Pro Leu Lys Ile Leu Ala His Asn Asn Phe Val
 275 280 285
 Gly Arg Leu Ile Gly Lys Glu Gly Arg Asn Leu Lys Lys Ile Glu Gln
 290 295 300
 Asp Thr Asp Thr Lys Ile Thr Ile Ser Pro Leu Gln Glu Leu Thr Leu
 305 310 315 320
 Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys
 325 330 335
 Ala Lys Ala Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu
 340 345 350
 Asn Asp Ile Ala Ser Met Asn Leu Gln Ala His Leu Ile Pro Gly Leu
 355 360 365
 Asn Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro
 370 375 380
 Pro Thr Ser Gly Pro Pro Ser Ala Met Thr Pro Pro Tyr Pro Gln Phe
 385 390 395 400
 Glu Gln Ser Glu Thr Glu Thr Val His Leu Phe Ile Pro Ala Leu Ser
 405 410 415
 Val Gly Ala Ile Ile Gly Lys Gln Gly Gln His Ile Lys Gln Leu Ser
 420 425 430
 Arg Phe Ala Gly Ala Ser Ile Lys Ile Ala Pro Ala Glu Ala Pro Asp
 435 440 445
 Ala Lys Val Arg Met Val Ile Ile Thr Gly Pro Pro Glu Ala Gln Phe
 450 455 460
 Lys Ala Gln Gly Arg Ile Tyr Gly Lys Ile Lys Glu Glu Asn Phe Val
 465 470 475 480
 Ser Pro Lys Glu Glu Val Lys Leu Glu Ala His Ile Arg Val Pro Ser
 485 490 495
 Phe Ala Ala Gly Arg Val Ile Gly Lys Gly Gly Lys Thr Val Asn Glu
 500 505 510
 Leu Gln Asn Leu Ser Ser Ala Glu Val Val Val Pro Arg Asp Gln Thr
 515 520 525
 Pro Asp Glu Asn Asp Gln Val Val Val Lys Ile Thr Gly His Phe Tyr
 530 535 540
 Ala Cys Gln Val Ala Gln Arg Lys Ile Gln Glu Ile Leu Thr Gln Val

545 550 555 560

Lys Gln His Gln Gln Gln Lys Ala Leu Gln Ser Gly Pro Pro Gln Ser
 565 570 575

Arg Arg Lys

```
<210> 450
<211> 1743
<212> DNA
<213> Homo sapiens
```

400> 450							
atgaacaaagc	tgtatatcgg	aaacctcagc	gagaacgcgc	ccccctcgga	ccctagaagt	60	
ttctccaagt	acgccaaagt	cccggtgtcg	gagaccttc	tgtggaagac	tggctacggc	120	
tctgttgact	gccgcgacga	gagctggggc	ctacaggcca	tcggaggcgt	ttcaggttaa	180	
atagaattcg	acgggaaacc	ctagaagtgt	gcgaactcgt	tcocaaaag	ccaaaggatt	240	
cggaaacttc	agatagcaaa	tatccgcctc	catttaccgt	ggagggtgct	gggatagtta	300	
ctgtctcagt	atggagtgtg	ggagactgtg	gcacaagtga	acactgactc	ggaaactgca	360	
gttgtaaatg	taacctattc	cagtaaggac	caagctagac	aagcactaga	caaaactgat	420	
ggattctcgt	tagagaaatt	caaccttgaa	tgccctata	tcctctatga	aagccggccc	480	
cgacaaaacc	ccctgcagca	gcccgaggtg	ctgcggggcg	tgtggcgacg	gggtctctca	540	
aggcaggggc	ctccaggatc	cgatctcaag	cagaaacctc	gtgatttgcc	ttctgcgcgt	600	
ctgtgttcgt	cccaatttgg	tgtgacccat	atagaaaag	agattgtcac	cattcggaac	660	
atgcccaaac	agaccacgtc	taaaattcgt	gtccacccta	atgaaaaatg	gggggctgct	720	
cgacaaatga	ttaactactc	ctctactcct	gaaggcaact	ctcgcggtcg	taagtctatt	780	
ctggagatta	tgcataaagg	agctcaagat	ataaaattca	cagaagagat	ccccctgaag	840	
atttttagct	ataataactt	tgtgtgcagc	acttattgta	aaggaaggaa	aaattctaaa	900	
aaaattgagc	aagacacaga	actctaaact	ccgatatact	caatgcagga	attgacgtcg	960	
tataattcag	aacgcactat	tacagttaaa	ggcaattgtg	agacattgtc	caaaagtgcg	1020	
gaggagatga	tgaagaaaaa	cagggagctc	tataagaatt	attatgtctc	tatgaattct	1080	
caagcacatt	taattctcgt	attaaactct	aacgcottgg	gtctgttccc	accocattca	1140	
gggatgccac	ctcccaccct	aggggccctc	tgcgccatga	ctctctccct	ccccgcattt	1200	
gcgaactcag	aaacgcgagc	tgttcatctg	tttatccaga	ctctatcact	cggtgcacat	1260	
attcgccagc	acggcgcaga	ctatcaagac	cttcttcgtc	tgtgtggagc	tcbaattaat	1320	
attgtctcag	cgggaagcac	agatgcctaa	gttgagatgt	tgattatcac	tggaacacca	1380	
gaggtccact	tcaaaggtca	gggaagaatt	tgttgaaaac	ttaaaagtga	acaacttggt	1440	
atgctctaa	aagaagctga	ccttgaagct	catatcagag	tgccactcct	tgctgtgtgc	1500	
agagttattg	gaaaaggagg	caaaaacggt	aatgaacttc	agaatttgtc	aagtcgaa	1560	
gttctgttgc	ctcgtgacac	gacactcgtg	gagaatgacc	aagtgattgt	caaaataact	1620	
ggtcactctc	atgcttgcca	ggcttccgac	agaaaaattc	aggaattctc	gactcaggtg	1680	
acagcagcac	aacaacagaa	ggctctgcac	agtgggaccac	ctcagtcag	acggaagttaa	1740	
taa						1743	

```
<210> 451
<211> 25
<212> PRT
<213> Homo sapiens
```

<400> 451
Leu Gly Lys Glu Val Arg Asp Ala Lys Ile Thr Pro Glu Ala Phe Glu
5 10 15

Lys Leu Gly Phe Pro Ala Ala Lys Glu
20 25

<210> 452

<211> 25

<212> PRT

<213> Homo sapiens

<400> 452

Lys Ala Ser Asp Gly Asp Tyr Tyr Thr Leu Ala Val Pro Met Gly Asp
5 10 15

Val Pro Met Asp Gly Ile Ser Val Ala
20 25

<210> 453

<211> 16

<212> PRT

<213> Homo sapiens

<400> 453

Pro Asp Arg Asp Val Asn Leu Thr His Gln Leu Asn Pro Lys Val Lys
5 10 15

<210> 454

<211> 20

<212> PRT

<213> Homo sapiens

<400> 454

Lys Ile Ala Pro Ala Glu Ala Pro Asp Ala Lys Val Arg Met Val Ile
5 10 15

Ile Thr Gly Pro
20

<210> 455

<211> 20

<212> PRT

<213> Homo sapiens

<400> 455

Pro Asp Glu Thr Ala Ala Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly
5 10 15

Arg Arg Gly Leu
20

<210> 456

<211> 20

<212> PRT

<213> Homo sapiens

<400> 456

Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr Cys Ala Lys Ala Glu

5 10 15

Glu Glu Ile Met
20

<210> 457
<211> 20
<212> PRT
<213> Homo sapiens

<400> 457
Ala Phe Val Asp Cys Pro Asp Glu Ser Trp Ala Leu Lys Ala Ile Glu
5 10 15

Ala Leu Ser Gly
20

<210> 458
<211> 20
<212> PRT
<213> Homo sapiens

<400> 458
Ile Arg Lys Leu Gln Ile Arg Asn Ile Pro Pro His Leu Gln Trp Glu
5 10 15

Val Leu Asp Ser
20

<210> 459
<211> 20
<212> PRT
<213> Homo sapiens

<400> 459
Ala Gln Gln Asn Pro Leu Gln Gln Pro Arg Gly Arg Arg Gly Leu Gly
5 10 15

Gln Arg Gly Ser
20

<210> 460
<211> 20
<212> PRT
<213> Homo sapiens

<400> 460
Asp Val His Arg Lys Glu Asn Ala Gly Ala Ala Glu Lys Ser Ile Thr
5 10 15

Ile Leu Ser Thr
20

<210> 461

<211> 20
<212> PRT
<213> Homo sapiens

<400> 461
Leu Tyr Asn Pro Glu Arg Thr Ile Thr Val Lys Gly Asn Val Glu Thr
5 10 15
Cys Ala Lys Ala
20

<210> 462
<211> 20
<212> PRT
<213> Homo sapiens

<400> 462
Glu Glu Glu Ile Met Lys Lys Ile Arg Glu Ser Tyr Glu Asn Asp Ile
5 10 15
Ala Ser Met Asn
20

<210> 463
<211> 20
<212> PRT
<213> Homo sapiens

<400> 463
Leu Asn Ala Leu Gly Leu Phe Pro Pro Thr Ser Gly Met Pro Pro Pro
5 10 15
Thr Ser Gly Pro
20

<210> 464
<211> 20
<212> PRT
<213> Homo sapiens

<400> 464
Lys Ile Ala Pro Ala Glu Ala Pro Asp Ala Lys Val Arg Met Val Ile
5 10 15
Ile Thr Gly Pro
20

<210> 465
<211> 18
<212> PRT
<213> Homo sapiens

<400> 465
Thr Gly Tyr Ala Phe Val Asp Cys Pro Asp Glu Ser Trp Ala Leu Lys Ile
5 10 15

Glu

<210> 466
<211> 11
<212> PRT
<213> Homo sapiens

<400> 466
Phe Val Asp Cys Pro Asp Glu Ser Trp Ala Leu
5 10

<210> 467
<211> 33
<212> DNA
<213> Homo sapiens

<400> 467
ttcgtggact gcccgacga gagctgggcc ctc 33

<210> 468
<211> 24
<212> PRT
<213> Homo sapiens

<400> 468
Ile Pro Asp Glu Met Ala Ala Gln Gln Asn Pro Leu Gln Gln Pro Arg
5 10 15

Gly Arg Arg Gly Leu Gly Gln Arg
20

<210> 469
<211> 24
<212> PRT
<213> Homo sapiens

<400> 469
Ile Pro Asp Glu Thr Ala Ala Gln Gln Asn Pro Ser Pro Gln Leu Arg
5 10 15

Gly Arg Arg Gly Pro Gly Gln Arg
20